



# SURGERY

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*GASPAR TALIACOTIUS*  
(1546-1599)

From painting in the Istituto Ortopedico Rizzoli, Bologna, Italy

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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NUMBER I

### THE TRANSPLANTATION OF SKIN AND SUBCUTANEOUS TISSUE TO THE HAND

SUMNER L. KOCH, M D , F A C S , Chicago, Illinois

THE surgeon who transplants skin and subcutaneous tissue is indebted to many men whose experiments and discoveries have made possible the results which he accepts today as a matter of course. It is fitting that we should pause and pay our tribute to the surgical pioneers to whom we are so greatly indebted, and it is interesting to inquire what sort of men these individuals were whose names have been upon our tongues so often, but concerning whose lives and personalities so little is recorded.

As with many surgical procedures the origin of the idea of transplanting tissues from one part of the body to another is shrouded in mystery, but it dates back many centuries. In some of the earliest records,<sup>1</sup> it is said, the

From the Division of Surgery, Northwestern University Medical School. Read before the Minneapolis Surgical Society, Minneapolis, Minnesota, February 1, 1940.

"... plastic surgery was practiced in ancient India and Egypt as is shown by the sacred writings of India and in Ebers' *Papyrus* in both of which rhinoplasty is mentioned as a well known procedure." (*Plastic Surgery*, J S Davis, p 1.)

The first part of this statement is correct. In the *Sushruta Samhita* (200 B C - 300 A D) the surgeon is advised to repair the defective lobe of the ear with a "patch of living flesh from the cheek." "with one of its ends attached to its former seat" and to repair the injured nose with "a patch of living flesh" sliced off from the region of the cheek.

In *Commentaries and Annotations on the Sushruta Samhita* F Hessler quotes (*Die Literatur und Geschichte der plastischen Chirurgie*, p 59). The careful doctor takes [as a pattern] the leaf of a plant the size of the nose, cuts a flap from the cheek according to the pattern laid upon it, but leaves the flap attached at one place. He quickly puts the [new] nose in place after he has incised the edges, fastens it in the proper position

restoration of the nose by the use of pedunculated flaps from both forehead and cheek is referred to as a well recognized procedure, and it is probable that the desire for restoration of form as well as function was as dominant an impulse in the injured East Indian and Egyptian of 5000 years ago as it is in the war veteran and glamour girl of today.

Celsus, Galen, and other writers of the first centuries after Christ described the repair of defects of ears, noses, and lips by the aid of flaps from the adjacent tissues, and then followed a hiatus of centuries, as far as progress in the transplantation of tissue is concerned, before the appearance of a small volume, *De curtorum chirurgia per insitionem* (Surgery of the Mutilated by Grafting) (Fig 1), in 1597

with a good bandage carefully inserts two small tubes of appropriate size [as breathing spaces] elevates it, and strews over it dust of red sandalwood, sweet wood and antimony. Then he covers it with white cloth and moistens it often with oil of sesame

"When the transplanted flap is united the pedicle is divided. If the nose is too small one attempts to make it grow; if it is too large one reduces it to the proper size."

A careful reading of Cyril P. Bryan's and of B. Ebbell's translations of the German version of the *Papyrus Ebers* (early sixteenth century B C) reveals no mention of rhinoplasty nor of any surgical procedure remotely resembling it.

Bryan states (page 76) "Skin grafting it may be shortly said formed no part of the accomplishments of the medical practitioner in Ancient Egypt" and Ebbell says (p 17) "Suturation is not mentioned at all so it has surely not been used."

In the Edwin Smith Surgical *Papyrus*, a seventeenth century B C copy of a treatise written in the Pyramid Age (3000-2500 B C) 48 surgical cases representing lesions of the upper half of the body are discussed in considerable detail. Here also no mention is made of skin grafting or transplantation of tissue.

again focused the attention of the surgical world on this problem.

One could point many a moral from the altar created by this volume—the far reaching importance of the discovery of printing, the forceful stimulus of war and pestilence to surgical progress, the value of illustrations in medical and surgical literature, the homage that is often given to the man who first records for mankind rather than to him who conceives a new idea but fails to tell it to the world in a voice that can be heard.

Gaspar Taliacotus or Tagliacozzi (1546-99) of Bologna (frontispiece) the author of the book in question lived in the stirring years that followed the discovery of the New World. He studied at the University of Bologna under Jerome Cardan (Geronimo Cardano) best known for his treatises on arithmetic, algebra, and natural history. He received the degree in philosophy and medicine at the age of 24. Six years later he was admitted to membership in the college of medicine and became a professor in the University of Bologna. Wars, disease, man's inhumanity to man brought him abundant opportunity for the exercise of his surgical skill. In one of their satirical essays in the *Teller*, Addison and Steele stated (though obviously in jest) that Taliacotus at one time had as patients under his care 12 French marquises, 20 German counts, 100 Spanish noblemen.

Taliacotus' work is divided into two books. The first includes an elaborate introduction with references to the poets, the fathers, and the scriptures; a discussion of the principles involved in the transplantation of tissue; a theoretical consideration of the choice of tissues to be used in the restoration of ears, lips, and noses; and in the nineteenth chapter, references to the work of Galen, Celsus, Paul of Aegina, of Alexander Benedictus and of his contemporaries—Fallopian, Vesalius, Paré and Schenk. In the second book the repair of defects of the nose with the aid of a delayed pedunculated flap from the arm is described in detail. The instruments required, the technique of the operation, the duties of the surgeon's assistants and the postoperative care of the patient are discussed at length.

Twenty-two beautiful woodcuts by Francesco Capello of Modena, a decorator of churches and an illustrator of books, picture the various steps of the operation and the apparatus used to hold the arm immobilized alongside the nose while the transplanted flap is developing a new blood supply (Fig. 2).

Although Taliacotus is often referred to as the originator of the Italian method of rhinoplasty, his own writings indicate that the principles involved had been recognized long before and that the operation as he performed it had been practiced for more than a century. Records dating back as far as 1442 mention Branca, a Sicilian surgeon, as practicing a method for replacing defects of the ears, lips, and nose, and his son Anthony is referred to as "a celebrated surgeon who restored ears, lips and noses." Vincent Vianus, also called Vioneus, Boianus, and Boiani, a surgeon of Tropaes, together with a nephew Bernard and the latter's son Peter who died in 1571 were also distinguished for repairing defective lips and noses.

Alexander Benedictus, a native of Legnano who taught medicine in Padua before 1495, has left a record of the technique of rhinoplasty which was published in 1497 exactly 100 years before the appearance of Taliacotus' work.

"In our time skillful persons have taught us how to rectify deformities of the nose. Portions of flesh, cut from the arm of the patient, formed into the shape of nostrils, and added to the trunk of the nose are very common seen. They dissect the upper skin of the arm with a razor, and, then, joining off the remaining edges of the nostrils, or if necessary cutting them off, they bind the arm to the head, in order that when it may draw toward the head, the wounds having conglutinated, they take flesh from the arm with the knife, much as is wanted for the restoration of the nose, which they accomplish for the kindred cures of the nose now. With the flesh which is newly acquired, while hairs sometimes grow on the skin, because of its origin on the arm, in this manner with admirable art new noses are reformed, the open nostrils and, if held permit, natural respiration is subjected to our ill. It is to be added, in the mean time, that these artificial noses hardly endure severe winter and, if either I or persons to see them gently lest they be torn off from the trunk.

Fallopian who died in 1563 also described the operation. Paré referred to it in 1561 and

G A S P A R I S  
T A L I A C O T I I

B O N O N I T A S I S.

PHILOSOPHI ET MEDICI PRAECLARISSIMI

THEOLOGICAL STUDENTS, & ALUMNI OF THE SYNOPSIS SEMINARY, PAID PROPORTION

De Curtorum Chirurgia per Infectionem,

LIBRI DV

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exemplaire et j'adresserai aux Thiers, aux Pons, aux premiers et aux  
autres, les premiers et les autres, les premiers et les autres.

Ad Res Cuius Instrumentum omnium a. g. e. d. i. t. e. n. u. m.  
I. n. o. b. i. s. & T. a. b. u. l. i. s.

Cette notice qualifie les expéditions de la notice précédente et indique les documents qui y sont joints.

Cam Pinalogys Sonoma Pacific Cafetera Mexicana Co. 4  
Hesperian, Sonoma Youth, 5-12, 1971



VENETIÆ. M D XCVII.

Apud Gasparum Bindonum juniorem.

Fig. 1 Title page of the first edition (Bindonus edition) of Tiliacotus' *De Curtorum Chirurgia per Institutionem*

Vesalius in his *Chirurgia Magna* (1569) discussed the problem of restoration of the nose and gave an imperfect account of the operation.

Although Taliacotius acknowledged his indebtedness to those who had gone before him his comprehensive discussion of the problems involved and his accurate and beautifully illustrated description of the operation of rhinoplasty entitle him to the honored place he holds in surgical history.

At his death at the age of 53 years, November 7, 1599, the magistrates of Bologna placed a statue in his honor in the anatomical theatre of the University, and the faculty a marble tablet with the following inscription

36

CHIRVRG CVRT

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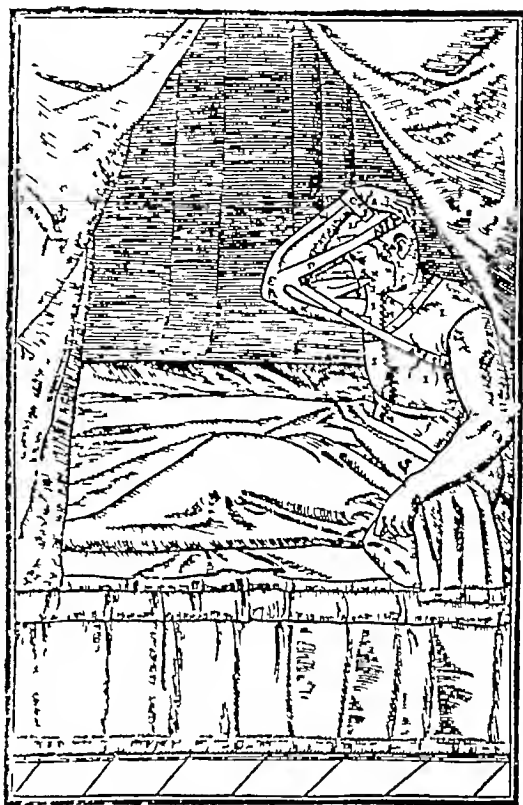


Fig 2 Illustration from Tiliacotius' *De Curtorum Chirurgia per Institutionem*, illustrating his method of immobilizing the upper extremity beside the head

“To Gaspar Tachozzo, citizen of Bologna, and a celebrated philosopher and physician of his age, well acquainted with the anatomy of the whole human body, which he frequently dissected before a public assemblage of the most learned men, and demonstrated with admirable eloquence, method, and doctrine, pouring light upon the most obscure parts Readers and Medical Professors' the Faculty of Bologna, in testimony of their gratitude, and to perpetuate the remembrance of it, have raised him this monument ”

It is said, however, that after his burial in the church of St Giovanni Battista voices were soon heard proclaiming "Taliacotius is damned," and that to prevent desecration of hallowed ground his body was exhumed and cast into the outer darkness.



In the years following Taliacotius' death, because of the influence of the clergy who considered such operations as meddling with the handiwork of God" (Garrison) and the interdiction of face repairing by the Paris Faculty in 1788 plastic surgery fell into disrepute and not until the nineteenth century did definite progress again take place. In the meantime Taliacotius' teachings were forgotten and if they were sometimes recalled to mind it was with doubt as to their truth with *misrepresentation and often with ridicule*.<sup>1</sup>

In the nineteenth century along with the progress that took place in many phases of medicine and surgery interest in the transplantation of tissue was revived and this awakening was due both to a revival of interest in the teachings and achievements of Taliacotius and his contemporaries and to a belated recognition of the fact that in India for many years perhaps centuries, members of the potters' caste had repaired the ravages wrought by brutal warriors and potentates, and restored noses and lips with the aid of pedunculated flaps from the forehead. In 1816 Carpey a London surgeon, published an account of 2 cases of restoration of the nose by the Indian method,<sup>2</sup> and a few years later in Germany Dieffenbach (1792-1847) began his pioneer (work) in transplantations and experimental surgery on animals first essayed by John Hunter and Giuseppe Baroni (Garrison). The renaissance of plastic surgery thus begun reached its climax in the war years of 1914-1918.

The free transplantation of skin, as contrasted with the use of pedunculated flaps is a development of the nineteenth century. Although it has been said that in India the restoration of the nose with free grafts of skin and subcutaneous tissue was successfully accomplished I have been unable to find any definite record of it and if it was actually

carried out it remains an achievement that the surgeon of today has not been able to equal.

Of the men whose names have become associated with the transplantation of free grafts of skin—Reverdin, Lawson, Ollier, Thiersch, Wolfe, Krause—none of them probably would have considered himself a plastic surgeon or thought that his contribution to the subject of skin grafting would prove a float through posterity.

Although as early as 1804 Baroni successfully carried out in animals free transplantation of pieces of skin as large as 12.5 by 7.5 centimeters in size and although a partially successful transplantation of skin was reported by Dieffenbach in 1824 the first report which attracted the attention of the medical world was by JACQUES-LOUIS REVERDIN in 1869. On December 8th of that year he demonstrated to the Société Impériale de Chirurgie a patient on whom he had successfully carried out skin grafting with two small bits of epidermis raised with the point of a lancet from the patient's right arm.

Reverdin (1842-1929) was born in Geneva of a distinguished family whose forebears fled from France in 1799 to escape religious persecution. His grandfather was an artist and professor of design in the municipal college his father a distinguished architect his maternal grandfather a physician and naturalist. At the age of 20 he received the degree of bachelor of arts at the Academy of Geneva 2 years later the degree of bachelor of science and immediately afterward began the study of medicine in Paris. In the *concours* of 1865 he received the coveted appointment of *interne des hôpitaux* and for 4 years continued his studies in the hospitals of Paris. In 1869 he was awarded the gold medal of the *concours de l'internat* for his study upon the gravity of anthrax and of furuncles of the face and the privilege of continuing his

<sup>1</sup>Edward Zeis in *Die Literatur und Geschichte der plastischen Chirurgie* (page 47) cites the following report of J. F. Friedrich Dieffenbach from *Geneva and Zürich Journal*, 12, vol. 4, page 432.

In the case of an old woman whose left arm was completely amputated Dieffenbach cut in double-sized pieces of skin and excised them. He sutured, on the other day, each separately torn area with removal of the blood, on the same day. Hence if followed that one part of the body already becomes covered with the flaps (the wound) by means of connective tissue cellular tissue.

<sup>2</sup>Complete reconstruction of the resident group.

<sup>3</sup>Carpey presents and that in the eighteenth chapter of book one of *De Chirurgia*. Carpey's Taliacotius discovered the quantity of taking a flap from the arm of another person, and although he thought there was no reason to doubt that the skin of one person would unite with that of another he considered the operation impracticable and assumed that never been practiced. The same credulity which inspired the use of warts and pearls, and the sale of noses derived from the tissues of another person, which mortified when these latter exposed, still persists in the modern world.

Then beautifully presented small square volume illustrated with number of engravings by Charles Turner, contains well authenticated account of the history of the Indian and Indian methods of rhinoplasty. It is ascribed to Carpey for many of the facts recorded concerning Taliacotius and his work.

studies on the service of his choice. The following two years were spent on the surgical service of Dolbeau and Gosselin<sup>1</sup>, and during this period, in 1870, he acted as surgeon in chief of the ambulance established by the Swiss colony of the besieged city. During this period, also, Guyon, the distinguished urologist, presented in his behalf the report, referred to above, of Reverdin's experiments with small grafts, carried out on Guyon's service at l'Hôpital Necker.

In 1872, following the completion of his *internal*, in spite of the urgings of his teachers and the attractions of a surgical career in Paris, Reverdin returned to his native Geneva. Two years later he was appointed associate surgeon at the hospital of Geneva, and in 1876, chief surgeon. The same year he was appointed professor of external pathology and of operative medicine in the Faculty of Medicine, and for 34 years thereafter without interruption continued his work as a teacher.

In 1879 with his cousin, Auguste Reverdin, he founded a surgical clinic—an unusual venture, for specialization even in general surgery was still uncommon. In 1881 with Picot and Jean Louis Prevost he founded the *Revue medicale de la Suisse Romande* and for 38 years as editor and contributor continued to take an active interest in it.

Like every Swiss surgeon he was greatly interested in thyroid disease, a condition endemic in Switzerland. He had often noted in his patients the development of tardy and peculiar symptoms after thyroidectomy, and in 1882 he presented the results of his observations to the Société Médicale of Geneva, suggesting that the thyroid gland exerted an influence on the body hitherto unrecognized. Kocher corroborated Reverdin's observations and gave the name *cachexia strumipriva* to the symptom complex described by Reverdin.<sup>2</sup>

<sup>1</sup>Both men were keenly interested in the subject of infections of the hand. Gosselin maintained that deep infection invariably extended along the tendons sheaths. Dolbeau contended that it frequently resulted from extension along the lymphatics. Their discussions were often bitter and acrimonious. Both were right.

<sup>2</sup>Considerable controversy arose as to who deserved priority for the recognition of the relation between removal of the thyroid and post-operative myxedema, and the fact that the post-operative condition is identical with that resulting from aplasia of the thyroid described by Cullen in 1813. Macchiari says that Reverdin deserves the credit and that this fact was emphasized at the Conference Internationale du Centre at Ierne in August 1905. Osler says Kocher in 1883 reported that to of his first 100 thyroidectomies had been followed by a very characteristic

From 1882 until 1910 Reverdin continued his active clinical and investigative work. He was interested in practically every phase of general surgery and his many contributions included in addition to a number of papers on skin grafting and thyroid surgery such diverse subjects as umbilical hernia, coxofemoral disarticulation, hallux valgus, ether anesthesia, and the surgery of war wounds.

In 1910 at the age of 68 he resigned from his teaching and professional activities and devoted the remainder of his life to scientific writing and the pursuit of what had long been a favored avocation—the study of Lepidoptera. In this field also he attained distinction and became an honorary member of entomological societies of Philadelphia, London, Brazil, France, and Switzerland. He died “full of years and honors” January 9, 1929.

Reverdin's original paper on the subject of skin grafting appeared in the *Bulletin de la Société de Chirurgie*, December 15, 1869. He had previously noted the occasional spontaneous development of small islands of epithelium at the center of a raw surface, and the rapidity with which epithelization extended peripheralward from such islands. This observation led to the idea of hastening the healing process by the actual application of such islands over the granulating surface. The case reported was that of a man of 35 years who had sustained on October 16 an avulsion of skin and subcutaneous tissue from the left upper extremity from elbow to mid-forearm.

“On November 24th I raised with the point of a scalpel two small bits of epidermis from the patient's right arm. The first was very small, the second nearly a millimeter square, the small wound [at the donor site] showed only red oozing. I placed my two fragments in the middle of the wound, their deep surface in contact with the granulations, at a little distance from one another, and held them with a diachylon bandage. The following day the fragments were still in place in spite of very abundant suppuration, they appeared a little swollen and paler.”

Three days later a third graft of 3 or 4 square millimeters was applied to the wound.

picture to which he gave the name *cachexia strumipriva*, an observation which had already been made in the previous year by the Reverdin who also had recognized the relation of this change to the disease known as myxedema.



J. L. REVERDIN  
(Revue méd. de la Suisse Romande, 19, 1900)



GEORGE LAWSON  
(Brit. M. J. 1903, 10)

On December 1st the first two grafts had united as a result of the outgrowth of epidermis from their free margins. During the fol-

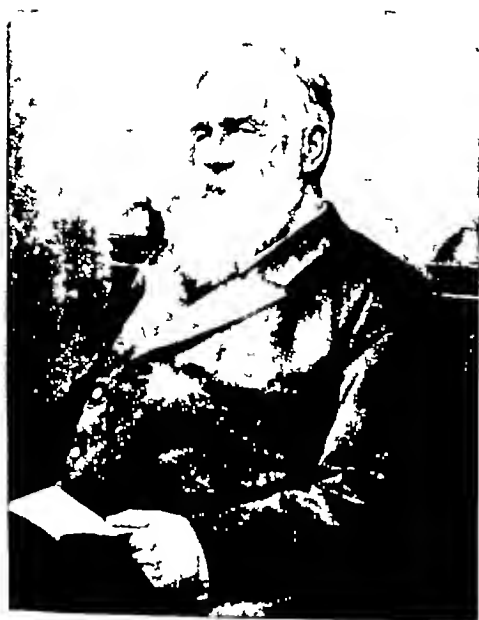
lowing days the epidermis continued to extend from the margin of the united grafts and from the margin of the third, and on December 7 they were united and formed a small white island exactly analogous to the border of epidermis which forms at the margins of a wound.

Reverdin's observations attracted wide attention, by no means entirely favorable for the possibility of erysipelas developing at the donor site was suggested as a serious danger. Nevertheless his method was promptly utilized by other European surgeons. On November 11, 1870 less than a year after the appearance of Reverdin's report C. D. Pollock reported before the Clinical Society of London 16 cases in which Reverdin's method had been utilized in an effort to secure healing of raw surfaces with the aid of small grafts. Of the 16 8 were successful, 2 partially successful, 6 were failures.



LOUIS N. E. L. OLLIER  
(1894-1905) (Le médecin de l'École de Chirurgie, 1906)

Immediately following Pollock's report is a brief paper which deserves attention. On the Transplantation of Portions of Skin for the Closure of Large Granulating Surfaces by C. FORGE LAWSON read November 11, 1870. With his paper Lawson presented 2 of 3 pa-



CARL THIERSCH

(Frontispiece *Carl Thiersch sein Leben* by Justus Thiersch  
Leipzig Barth 1922)



J. R. WOLFE

(*Chicago Clin Rev* 1893-94 3 113)

lients on whom operation had been carried out In the first patient with a large varicose ulcer of the leg he "transplanted a portion of skin from the inner side of the arm" In the second patient with a varicose ulcer 3 by 1 $\frac{3}{4}$  inches, he "transplanted a piece of skin from the inner side of the arm of the size of a four penny piece The new skin very shortly united, and granulations rapidly sprang from its circumference which closed the wound in about 18 days from the time of its transplantation" In the third case an ectropion of the upper lid was freed, the tarsal edges of the lids united, and 3 days later a piece of skin the size of a silver three penny piece "which I removed with a pair of scissors from the inner side of the arm" laid on the nasal side of the lid, as at that spot the granulations looked most vascular and healthy

In his conclusions Lawson states,

"The cases which I have related show that pieces of skin of the size of a sixpence can be easily engrafted on granulating surfaces, it remains for experience to decide how much larger portions can with safety be transplanted, and what are the conditions under which these transplantations can be most satisfactorily conducted When once these facts are thoroughly ascertained, the present treatment of

burns and of deformities arising from a large destruction of skin will be completely changed We shall no longer allow extensive granulating surfaces



FEDOR KRAUSE

(*Zentralbl f Neurochir*, 1938, 2 121)

t be closed over b an indra l g of the surrounding kin but shall freely tra pta t portions of skin from those parts of the body where there is re dundancy The conditions which seem to me es sential f the grafting of large portions of skin re—

That the new skin should be pplied t healthy gra elating surface

2 That kin en/ should be transplanted, and that special care should be taken that there is no fat adherent t it.

3 That the portion of skin should be ex cecutely d firmly applied to the granulating surface.

4 That the new skin should be kept in its new position without interruption.

Lastly—I would mention that the new skin thus engrafted, not only soon becomes vascular but it acquires sensibility

Although his name is rarely mentioned in connection with the transplantation of skin Lawson's report was the first account of the successful transfer of sizeable areas of skin as compared with the small grafts suggested by Reverdin and of whole thickness skin as well.

Lawson was born August 28 1831 He studied medicine at King's College in London and there became a student and later house surgeon to the distinguished Sir William Fergusson He became a member of the Royal College of Surgeons in 1852 and a fellow in 1857 In 1854 he was appointed staff assistant surgeon in the army medical corps and served for a year of the Crimean war

He was dispatched t Gallipoli and thence to Varna on the Black Sea I that foul and dilapidated port he suffered from a sharp attack of typhus fever Landing in the Crimea, La son as with the troops t the battle of Alma, and later on t the successful repulse of the Rumanians by the allied forces t Inkerman During the terrible winter of 54-5, when disease nd frost rough't yet greater ha roc than the Russian arms, La son was in the lines be fore Sebastopol The privations and horrors both inevitable and preventable, of that disastrous seige have been often told. Anesthetics ere then in their infancy and Lawson used to tell how his was the only inhaler in the outfit of the hol Third Division.

In 1855 he contracted typhoid fever which nearly proved fatal and was finally invalided home He resigned his army commission the following year The same year he was appointed to the surgical staff of the Middlesex Hospital, and served that institution with untainted devotion for 31 years.

In 1862 after serving as assistant to Bow man, he was appointed to the staff of the

Royal London Ophthalmic Hospital at Moorfields and continued to serve with distinction as ophthalmic surgeon until 1891 During this period he contributed a number of important papers to the Reports of the hospital and the Transactions of the Ophthalmological Society The titles of some of these papers—paracentesis of the cornea, amaurosis during pregnancy, traumatic cataract atropine irritation, primary epithelioma of the eyelid, tumors of the optic nerve—indicate the breadth of his scope and industry So interested was he in the subject of sympathetic ophthalmia that it became a tradition at the Middlesex Hospital that no matter what the subject with which he began his lecture he invariably concluded with a discussion of sympathetic ophthalmia. His textbook on *Injuries of the Eye Orbit and Eyelids* published in 1867 was considered a classic on the subject and his book on *Diseases and Injuries of the Eye* first published 2 years later passed through numerous editions.

As a general surgeon La son as both courageous nd painstaking fearless i undertaking any operation, however formidable f in his sound and sagacious judgment he had satisfied himself of its wisdom and justification. Though conservative b instinct he was a reformer in matters of hospital construction and in his scrupulous regard for cleanly surgery H was one of the first t discard the time honoured frock coat, soiled ith the blood stains of hundred operations in f vour of a suitable overall.

His outstanding ability as teacher and surgeon his constant thoughtfulness and kindly personality brought him both the admiration and devotion of his house surgeons, dresser and assistants. His patients, many of them from the poorest districts of London had frequent occasions to recall the thoughtfulness and generosity that enhanced his surgical skill and judgment. Not a few of the blind and the halt and maimed were sent from his outpatient desk to a neighbouring butcher with whom he had a running account for four pounds of beef

In 1886 he was appointed Surgeon-Oculist to Queen Victoria, and on retiring from the active staff of the Middlesex and Moorfields Hospitals he was elected consulting surgeon to both institutions.

Toward the end of his life a marked hypertrophy and dilatation of the heart resulted in serious circulatory deficiency and edema of the lower extremities, and for the last 18 months of his life he was confined to his arm-chair and never went to bed, so that the Southey tubes inserted in the subcutaneous tissues might drain properly. He died on October 12, 1903.

One of his five sons, now Sir Arnold Lawson, followed closely in his father's footsteps, and as an outstanding ophthalmologist has added still further distinction to the family name.

Like Reverdin, LOUIS XAVIER EDOUARD LEOPOLD OLLIER (1830-1900) came from a family with a background of scientific interest and achievement. Among his ancestors were a grand chancellor of the University of Toulouse, a number of magistrates, and four generations of physicians. His father was a physician in Vans in the department of Ardèche, where Ollier was born on December 2, 1830. A brother, a cousin, and two nephews were practitioners of medicine.

Ollier began the study of natural science at Montpellier, studied medicine at Lyons, and served as interne in the hospitals of Lyons. He received his doctor's degree at Montpellier in 1856. The following year, attracted by the great name of Claude Bernard and interested in the problem of growth and reproduction of bone as a result of the influence of his teacher, Bonnet, he went to Paris to attempt to settle the question of the osteogenetic function of the periosteum.

The dispute as to the bone forming power of periosteum was at its height. Duhamel, a young Frenchman, not a physician, had repeated the experiments of Belchier, the English surgeon, and noted the effect of feeding bran, soaked with madder, on the bones of fowls and pigs. He had noted that the laver of bone stained by the madder lay immediately under the periosteum and that an animal fed alternately with dyed and undyed food formed alternately red and white layers of cortical bone. Duhamel's observations were confirmed by the "brilliant experimental physiologist, the handsome courteous clever, and conceited Marie Jean Pierre Flourens"

(Keith, *Menders of the Maimed*, p. 130), but were vigorously contested by Albrecht von Haller, the Swiss professor of anatomy at the University of Goettingen "the master physiologist of his time" (Garrison). Haller had concluded from his experiments and observations that bone was a product of the arteries "which could lay down bone anywhere—with in cartilage or beneath the periosteum."

Ollier began his own experiments by raising a flap of periosteum from the surface of the tibia of a young rabbit, leaving the flap attached at its base and turning the free end of the flap over the deep flexor muscles of the leg. In six weeks the flap had become a loop of bone. He continued with other experiments, twisting the base of the flap to compress its blood vessels, dividing the pedicle three days after raising the flap, and finally transplanting free grafts of periosteum into the subcutaneous tissues of the thigh. In each case new bone was formed at the site of the transplant. He "entered Chauveau's laboratory a sceptic, when he had completed his first series of experiments he was convinced of the osteogenetic properties of periosteum."

In 1860, at the age of 30, he was called to the chair of clinical surgery at Lyons and appointed senior surgeon at the Hôtel-Dieu. After eight years of patient experimental investigations—on the periosteum, on the medulla, on the bone itself, on the effect of experimental fractures, on the effect of injury to the epiphyseal lines of growth—he published the results of his observations in two volumes entitled *Traité expérimental et clinique de la régénération des os et de la production artificielle du tissu osseux*, a classic on the subject of growth and development of bone.

Throughout his long career as professor of surgery at Lyons he continued his experimental and clinical studies with unflagging interest and energy. In a memorial written by Eugene Vincent in the *Archives provinciales de chirurgie* the list of contributions to surgical literature made by Ollier or inspired by him in the years from 1868 to 1900 occupies eleven pages. Almost one hundred of them were contributed by Ollier himself.

He died on November 25, 1900, in his seventieth year, in the midst of a family

reunion and only twenty four hours after he had performed a number of operations at the Hôtel Dieu and made the rounds of his surgical service. He had received almost every honor the surgical profession of his own and other nations could bestow upon him.

Ollier's contribution to the subject of skin transplantation appeared in 1872 in the *Bulletin de l'Académie de Médecine* under the title

Greffes cutanées ou autoplastiques. He went much farther in his conception of the problem than Reverdin, for he did not simply attempt to create new islands in granulation tissue from which epithelium might grow but carried out complete excision of scar tissue and its replacement with skin. He specifically stated that he used large grafts "4 6 8 centimeters square, and larger including not only the superficial layers of the skin but the entire derma — *comprenant non seulement les couches superficielles de la peau mais la totalité du derme*. For two years previous to his use of such *dermo-épidermiques* grafts he had used strips containing only a part of the derma, *lambeaux comprenant qu'une partie du derme* and in this respect also he had gone farther than Reverdin, but he favored grafts of whole thickness skin (*toute l'épaisseur de la peau*) for "*les résultats lui paraissent devoir être plus complets et plus persistants par la transplantation de la totalité du derme comme il la pratique aujourd'hui*"

One cannot read Ollier's paper carefully without realizing that he deserves credit for the first description of the graft of intermediate thickness and that he shares with Lawson the credit for the initial successful use of the graft of whole thickness skin. Finally it is interesting to note that he laid a free graft of periosteum from an amputated leg over a granulating surface, for he considered the connective tissue as the active element in the growth of a graft. We do not know the result of this procedure but it indicates that his interest in the transplantation of skin was closely related to his long continued study of periosteal transplants and bone growth.

CARL THIERSCH (1822-1895) belongs to the distinguished group of men who were responsible for the high esteem accorded to

German medical science during the last half of the nineteenth century. He was born in Munich April 20, 1822 studied there, and received the degree of doctor of medicine in 1843. After four years of study in Berlin, Vienna, and Paris he returned to Munich. In 1848 he was appointed professor in pathological anatomy and in 1853 professor. In 1850 he served as a volunteer surgeon in the second Schleswig Holstein campaign and during that interval was greatly influenced in his surgical outlook by Stromeyer the father of modern military surgery in Germany (Garrison).

In 1854 he was appointed professor of surgery at Erlangen and in 1867 to the chair of surgery at Leipzig. The years that followed constituted the golden age for the University of Leipzig. Carl Ludwig had become professor of physiology 5 years before Wilhelm His came from Basel 5 years later. The tribute of His to his two great contemporaries, published in the *Akademische Gedächtnisrede* and translated in Appleton's *Popular Science Monthly* is a graphic portrayal of the two men and of their contribution to Leipzig and to medical science.

Thiersch was a pioneer apostle of fresh air and sunshine in the treatment of surgical patients. The Jacob's Hospital built under his direction, was the first hospital in Europe constructed on the pavilion or barrack plan. Air and light, he said, are unpaid but in valuable assistant physicians. Lister's paper

On the Antiseptic Principle in the Practice of Surgery. It will be recalled was published in 1867 the same year that Thiersch was called to Leipzig. Thiersch was quick to recognize the importance of Lister's contribution and became one of his strong protagonists.

"When, soon after the opening of the hospital in 1871 Lister's beneficent methods of surgical treatment were made public, it was gain Thiersch, so at once recognized their enormous significance and advocated them with all his power. This beautiful hospital afforded him the best possible conditions for the carrying out and further development of the newly acquired methods, as well as for their introduction in the education of the younger medical generation. There he worked during the past twenty four years, not only as teacher revered by all, but also as faithful physician and he so loved his hospital that even during his time of suffering he occu-

pied himself ceaselessly with it, and one of the last wishes he expressed was that he might be able to return there once more" (Wilhelm His, *Carl Ludwig and Carl Thiersch*)

Thiersch's most important contributions were his monograph on epithelial cancer, his treatise on wounds and wound healing and on the transplantation of skin. His first paper was presented before the third Congress of the Deutsche Gesellschaft fuer Chirurgie April 9, 1874. He had utilized for experimental transplantation of skin an extensive ulcer of the leg of four years' standing, recurring in its entire extent after healing had once been secured with the aid of Reverdin grafts. Over this extensive ulcer he had applied centimeter square grafts at periods varying from 3 weeks to 18 hours before amputation. The amputated leg was injected with Gerlach's injection mass and the grafts studied with the help of fine sections stained by various methods.<sup>1</sup> Thiersch was able to demonstrate the vascularization of the agglutinated grafts as early as 18 hours after their application by "intercellular ducts which are immediately fed with blood from the granulation vessels and carry it into the vessels of the engrafted skin and back again." In the course of a few days, he stated, a few of the ducts were transformed into blood vessels while the remainder were obliterated. He noted that frequently the superficial portion of the graft became necrotic and sloughed, and that the deeper retained portion contained sweat glands. It was from these sweat glands, he assumed, that epithelium sometimes developed 1 or 2 weeks after apparently complete loss of the graft had taken place.

Thiersch recognized the fact that soft hypertrophic granulations formed an unsatisfactory bed upon which to lay a graft, and that even if healing took place the healed surface was incapable of withstanding trauma and often gave way as a result of slight injuries.

"Can this disadvantage be eliminated? Perhaps in the perpendicular section of the granulating tissue two definite layers can be distinguished: the under-

<sup>1</sup>In an obituary notice in the *British Medical Journal* (1895 II 1360) it was noted that Thiersch was a most dexterous microscopist, and that when section cutting and staining were in their infancy, he supplied Smith and Beck of Cornhill with marvellous slides of injected and stained specimens of normal and pathological tissues.

lying one with rather tensely drawn connective tissue, and above it a horizontally placed network of vessels. From this horizontal stratum of vessels and tissue, the much softer granulations, richly supplied with vessels, develop in perpendicular direction.

"If this portion becomes incapable of transformation into scar tissue, i.e., if the soft granulations, with their wealth of vessels, are not transformed into rigid, narrow scar papillae, with few vessels, the re-opening of the granulation closed by the skin graft is only a question of time. The only alternative, therefore, is elimination of the superficial portion of the granulation and implantation of the skin directly upon the tense underlying tissue. This substratum is exposed by sharp, horizontal incision, hemorrhage is permitted to run its course completely, and then the skin graft is placed upon this fresh wound surface, whose vessels and tissues are in excellent condition for immediate inflammatory adhesion."

In later papers (1886, 1888) Thiersch advised cutting or scraping off granulation tissue down to the firm underlying tissue before applying grafts over a granulating surface, cutting grafts with a razor blade in lamellae as thin as possible from the patient's own skin, and placing the grafts with overlapping edges to avoid scar formation. In preparing the field of operation he considered antiseptics a disadvantage and used only physiological salt solution.

His use of a graft to line a flap from the temple, intended to replace the upper lip, and of a graft to cover an extensive defect of the temple left after raising a pedunculated flap to cover the eyelids, the side of the nose and cheek indicates to what an extent he had visualized the possibilities of transplantation of skin.

JOHN REISSBERG WOLFE (1824-1904), like George Lawson, was an ophthalmic surgeon. He was born in Breslau but received his medical education at Glasgow University and the degree of doctor of medicine in 1856. After serving for some years as ophthalmic surgeon at the Royal Infirmary at Aberdeen, he returned to Glasgow and founded the Ophthalmic Institution in West Regent Street. When the St. Mungo's College Medical School was organized Wolfe became the first professor of ophthalmology.

After practicing with distinction for some years he moved to Melbourne, Australia, in 1893 and continued in the practice of his



specialty there for 8 years. He returned to Scotland in 1901 and died in Glasgow.

Wolfe's first report of the use of whole thickness skin as a graft appeared in the *British Medical Journal* (1875 2:360). He said:

"T. Gibson laid down the rule, which has ever since been considered as the primary law, *ad sine qua non* to the success of the operation, that the flap must retain its connection to the adjacent living structure by a pedicle which is to be severed only after complete union and cicatrization of the raw surfaces. This pedicle has, in my opinion, been a source of great embarrassment to surgeons and tended rather to retard the progress of plastic surgery. From my observations on transplantation of structures from the lower limb and on skin-grafting, as well as on plastic operations, I have long held it demonstrated that in most cases the pedicle is not essential, if indeed it do contribute anything to the vitality of flap. This being once established, we are henceforward free to choose our bit of skin from any part of the body we may find suitable.

"My next endeavour has been to eliminate the elements of failure. The principal cause of failure I find to be in the subcutaneous structures. If we wish a skin-flap to adhere to new surface by first intention or agglutination, we must be sure that it is cleared of all areolar tissue and properly fixed in its new place. The following case will illustrate the points referred to.

He then described the repair of an ectropion of the lower right eyelid by excising the scar, suturing the edge of the lid to the upper lid and covering the defect, 1 by 2 inches, with a graft from the forearm. After removing the graft "as close to the dermis as compatible with the integrity of the flap" from two-thirds of the graft, "with a cataract knife I sliced off the areolar tissue leaving a white surface. This part of the graft remained viable and healed without loss."

That part which was applied without previous preparation looked rather livid the first day, improved the next two days, the fourth day it began slightly to suppurate and, after a hard struggle for life, a portion of it only remained while the rest shrank.

Wolfe's essential contribution as indicated by the above quotation, was his insistence that all the subcutaneous tissue should be removed and that the graft should consist only of skin—a point that had already been emphasized by Lawson (p. 8). On so slender

a foundation does the name Wolfe-Krause graft rest.

FEDOR KRAUSE (1856-1937) who died only 3 years ago was both a general surgeon and a neurologic surgeon. He studied in Berlin, Halle and Frankfurt am Main and graduated at Berlin in 1879. Subsequently he worked in the ophthalmological clinic of Julius Hirschberg, under Robert Koch at the Imperial Board of Health and under Weigert at Frankfurt. From 1883 to 1889 he was an assistant of Volkmann at Halle, was appointed a resident instructor in 1887 and professor in 1889. In 1892 he was appointed chief of the surgical division at the municipal hospital of Altona, and in 1900 chief surgeon of the Augusta Hospital in Berlin.

"Graduated from the school of Richard Volkmann in Halle the same creative strength and the same artistic fervor bound him to his honored preceptor. Endowed with personality of sparkling vitality and associated with a distinguished and gifted preceptor during a period of rapid surgical progress he knew how to value these gifts and this good fortune (Behrend).

His scientific interests included such widely separated fields as ophthalmology, bacteriology, tuberculosis of the bones and joints, and plastic surgery. His outstanding contributions, however, were in the field of neurologic surgery. His inaugural thesis (*Habilitationschrift*) in 1887 was on the subject of malignant neuroma. In 1896 he published his monograph on trigeminal neuralgia and on the anatomy and histology of the trigeminal nerve. Four years before he had first devised the extradural approach to the gasserian ganglion through a bone flap raised from the temporal region and this approach carried out almost at the same time by Hartley of New York, was the essential factor in transforming what had been a difficult and dangerous operation into a relatively simple and safe procedure. Although Krause considered extirpation of the ganglion the operation of choice in the treatment of neuralgia, Behrend states that he had described preganglionic division of the nerve before the publication of Frazer and Spiller's paper on physiologic extirpation of the ganglion of Gasser in 1904.

In 1898, to relieve a patient suffering from an intractable tinnitus aurium he exposed and divided the auditory nerve by an approach through the posterior cranial fossa, and so laid the foundation for the surgical removal of tumors of the cerebellopontine angle. In a similar way the removal of a bullet from the roof of the right orbit just above the optic foramen in 1900 led to the transfrontal approach to the hypophysis.

At a time when the results of operation for brain tumor were disheartening, to say the least, Krause wrote

"The prognosis [of operations] varies according to the state of the neoplasms, the most unfavorable ones are the diffuse gliomas. Perhaps some day we shall reach the point of diagnosing these infiltrating gliomas with a fair degree of certainty. If this large percentage of inoperable neoplasms were eliminated from the field the operative prognosis would be essentially improved."

"We must not permit ourselves to become discouraged. Of course it requires a high degree of self-mastery to take up the knife again after a series of depressing failures in the hope that the next operation will have a satisfactory result. This field has merely been opened, the profession has freed itself from I. von Bergmann's view, to the effect that for the most part the brain tumors in the sensory-motor region are the only ones to be considered for operative treatment, but much still remains to be done."

His *Chirurgie des Gehirns und Rückenmarks*, published in 1911, and *Allgemeine Chirurgie der Gehirnkrankheiten*, published in 1914, were recognized as outstanding and fundamental contributions in the field of neurologic surgery.

Krause's paper on transplantation of skin was presented before the twenty-second congress of the *Deutsche Gesellschaft fuer Chirurgie* April 13, 1895. After dwelling briefly on the disadvantages of the pedunculated flap and the inadequate results obtained from the use of Thiersch grafts he described the favorable results obtained from the use of more than 100 whole thickness grafts used in 21 cases of grave ulcer of the leg and of defects of the face resulting from excision of cancerous growths or lupus. Of the more than 100 grafts, some of them 20 to 25 centimeters long and 6 to 8 centimeters wide, only 4 were completely lost. He stated that he followed "Wolfe's procedure" using only the cutis together with the

epidermis." He emphasized as matters of chief importance "complete asepsis, dry operation, and careful checking of hemorrhage, by means of compression, in the parts to be covered." He rarely sutured the graft to the margin of the defect but depended upon smooth and careful bandaging to hold it in place. The original dressing was left in place for 3 or 4 days and removed with extreme care to avoid separation of the graft. Complete healing, he stated, required from 3 to 6 weeks.

Undoubtedly Krause deserves credit for popularizing the use of grafts of whole thickness skin and emphasizing the wide indications for their use. From the standpoint both of originality and priority it would seem, however, that the graft of whole thickness should be called the Lawson-Ollier graft rather than the name by which it is referred to in most textbooks of surgery.

In paying our tribute to those who have gone before it is only right to add that every surgeon of today owes a great debt to two men who after long and successful careers are still actively interested in the teaching and practice of surgery. The contributions of Blair and Davis to the problem of transplantation of skin and subcutaneous tissue are too well known to require detailed comment. They will be referred to frequently in the concluding chapter of this paper.

**EDITOR'S NOTE.** The second and final chapter of this paper will appear in the next issue of this journal.

#### HISTORICAL REFERENCES

1. BAPONIO. *Degli Innesti Animali*. 1804 (cited by Garrison).
2. BREHMER, C. M. *Ieder Krause und die Neurochirurgie*. *Zentralbl. f. Neurochir.* 1938, 2: 122-127.
3. CARRIE, J. C. An account of two successful operations for restoring a lost nose from the integuments of the forehead, in the cases of two officers of His Majesty's Army, to which are prefixed historical and physiological remarks on the nasal operation, including descriptions of the Indian and Italian methods. London: Longman, Hurst, Rees, Orme and Brown, 1810.
4. CRISTO. A translation of the eighth book of Aulus Cornelius Celsus by G. F. Colclough, ed. London, 1811.
5. DAVIS, J. S. *The Principles and Practice of Plastic Surgery*. Philadelphia: P. Blakiston's Son & Co., 1909.
6. THOMAS LARSEN. Translated from the German version by Carl B. Brown. London: George Allen and Unwin, 1910.

- 7 THE PAPYRUS EBERS. The Greatest Medical Document. Translated by T. Ebbell. Copenhagen Levin and Munksgaard, 1917.
- 8 FRAMER, C. H., and SPILLER, W. O. Physiologic extirpation of the ganglion of Gasser. *J. Am. M. Ass.* 1904, 43, 943-947.
- 9 HIR, WILHELM. Carl Ludwig and Carl Thiersch. Appleton. Pop. Sci. Month., 808, 5, 338-353.
- 10 KEEFE, ARTHUR. *Masters of the Maimed*. London Oxford University Press, 9 p.
- 11 KRAUCK, F. Ueber die Transplantation grosser ungestillter Hautlappen. *Verhandl. d. deutsch. Gesellsch. f. Chir.* Berl., 893, 23, 46-51.
- 12 LAWSON, G. OWEN. On the transplantation of portions of skin for the closure of large granulating surfaces. *T. Clin. Soc. Lond.* 87, 4, 49-53.
- 13 Idem. *Obituary Brit. M. J.* 1903, 9-10.
- 14 MACHARD Jacques-Louis Reverdin. *Schweiz. med. Wchnschr.* 1903, 39, 384-386.
- 15 OLLIER. Des grandes cutanées autoplastiques. *Bull. Acad. de med. Par. ad ser.* 87, 243-246.
- 16 POLLOCK, G. D. Cases of skin grafting and skin transplantation. *T. Clin. Soc. Lond.* 1897, 4, 37-40.
- 17 REVERDIN, J. L. *Greff épidermique. Expérience faite dans le service de M. le docteur Guyon à l'hôpital Necker*. *Bull. Soc. imp. de chir. Par. ad ser.* 870, 5, 55.
- 18 SARNEY, P. J. Hindu medicine and its antiquity. *Ann. Med. Hist.* 93, 3, 3-324.
- 19 THE EDWIN SMITH SURGICAL PAPYRUS. Published in facsimile and idiosyncratic transliteration. Its translation and commentary in two volumes. James Henry Breasted. Chicago University of Chicago Press, 1930.
- 20 SURENDRA SAKHIA, an English translation based on original Sanskrit text. Edited by Ka. Ina. Kneja Lal Bhabhagrana. Calcutta, 1907.
- 21 TREITSCHE, C. Ueber die feineren anatomischen Veränderungen bei Aufhebung im Haut und Granaulationen. *Verhandl. d. deutsch. Gesellsch. f. Chir. Berl.* 874, 5, 69-75.
- 22 Idem. Ueber Hauteröffnung. *Zentralbl. f. Chir. Leipzig* 1886, 3, 7-8.
- 23 Idem. Vorrichtung von Perforator, an denen nach seiner Methode eine Hauteröffnung gemacht werden ist. *Verhandl. d. deutsch. Gesellsch. f. Chir. Berl.* 1888, 7, 60-67.
- 24 VALENT, EDUARD. La Professeur Ollier. *Arch. prov. de chir.* 90, 34.
- 25 WOLFE, JOHN R. A new method of performing plastic operations. *Brit. M. J.* 875, 360-36.
- 26 Idem. The transplantation of thymus. *Chicago Ch. Rev.* 305, 83-83.
- 27 Idem. Editorial. *Chicago Ch. Rev.* 303-04, 34-5.
- 28 ZEIS, EDUARD. Die Literatur und Geschichte der plastischen Chirurgie. Leipzig W. Engelmann, 1863.



mechanization of war with its increased mobility presents new problems in the collection and transportation of wounded. The increasing range of artillery fire combined with the mobility of the front and the ubiquity of the airplane in turn tends to decrease in type and amount the surgery permissible at the front.

**Débridement** Ambrose Paré was one of the first to oppose cauterization of wounds produced by missiles projected by gunpowder. In the oft quoted phrase "he layed the ghost of poisoned wounds from gunpowder and determined never again to burn thus so cruelly the poor wounded by arquebuses."

Although as early as 1897 a German surgeon, P. L. Friedrich, published experimental work on the treatment of contused wounds as if they were neoplasms the factor of vitality of tissues as the decisive element in infection has not been given its due importance (65-66). In the Franco-Prussian War only 9 per cent of the wounds were caused by shell-fire and approximately 90 per cent by bullets (43). With the development of modern warfare the ratio has been almost completely reversed. Approximately 75 to 80 per cent of all wounds in modern war occur as a result of low velocity projectiles from artillery fire. The type of wound commonly received, therefore is lacerated and contused usually contaminated by foreign bodies and requires extensive débridement to facilitate its healing and to avoid systemic infection. Because of the frequency with which débridement is done it has come to be known as "The Evacuation Hospital Operation." Evacuation hospital surgeons soon become specialists in débridement, but if their special training must be secured at the expense of the early wounded as in the last war it will be unfortunate (13). Leriche has stated also that débridement was accomplished by surgeons of the last war only after considerable experience and error. Inasmuch as "new hands" will take care of the wounded in future wars, it is important that the principles of débridement be taught to civilian surgeons. An appeal has been made in the regular army of the United States for careful instruction to all medical officers in "traumatic surgery" (39).

Judgment is the prime requisite for good results. From his experiences in the Spanish

Republican Army A. Tudor Hart emphasizes that the success or failure of any débridement depends on the persistence in the wound of no viable tissue or gross foreign matter. The ideal for which one must strive is to make a clean wound out of a dirty one. This is accomplished by the excision in mass of all torn, crushed discolored and non-contractile muscle along with loose bodies and bone and requires a sound knowledge of anatomy. In general primary closure of these wounds is undertaken only if the skin edges come together without tension and when the wound is less than 12 hours old. The indiscriminate use of tourniquets caused much damage in the last world war (68). Infection, massive gangrene, pain, tissue ischemia, and gas gangrene have all been attributed to the careless use of the tourniquet.

Ogilvie, in an excellent discussion on the treatment of wounds, carefully divides the progress of wound infection into two stages: contamination and infection. In the first stage (contamination) bacteria which have been carried in by the agent inflicting the wound lie on its surface in bits of dirt, clothing or metal fragments, or in the blood clot. This is the stage in which the bacteria can be removed by thorough mechanical cleansing. In the second stage (infection) the bacteria profiting by the supply of culture medium available to them in the dead matter, blood-clot, lymph and damaged muscle have multiplied and started to invade the host. For practical purposes the stage of contamination may be looked upon as lasting 12 hours before it passes into that of infection. When the organisms are few the available culture medium scanty and the surrounding tissues healthy the state of the patient's skin and clothes and the appearance of the wound will aid in an estimation of the probable degree of infection. Doubt as to the condition of the wound should incline one to pessimism rather than to mistaken optimism.

Levaditu (27) working with the French Army has made bacteriological studies on war wounds, both in 1914-1918 and in the current war. Of 317 cultures just taken, 32 per cent contained 3 species of organisms, 19 per cent contained 1 species, 19 per cent contained 4 spe-

cies, 23 per cent contained 5 or 6 species, and 7 per cent were sterile. The species most generally observed were staphylococci, 85 per cent, Friedlaender's bacillus, *Clostridium welchii*, streptococci, colon group, *Bacillus pyocyaneus*. He states that strong doses of -p-aminophenyl sulfamides applied *in situ* in powder form or in glycerine have had a remarkable prophylactic effect.

Col Leon Colebrook (28) estimates that streptococci are responsible for at least 70 per cent of all deaths due to infection of wounds. Of 49 positive blood cultures, 44 were hemolytic streptococci. Fifteen per cent of all wounds culture streptococci within 12 hours and in a few days the percentage is much larger—up to 90 per cent. It seems, therefore, that if sulfanilamide were present in the circulating blood at the time the organism reaches the tissue an infection might be prevented. Since a single prophylactic dose is excreted in 10 to 20 hours, the following dosage is advocated by Fuller and James:

1st dose 1.5 grams dissolved in 100 cubic centimeters of 1 per cent hot citric acid solution or hot lemon juice  
 2nd dose 0.5 gram without dissolving to delay absorption, 2 hours later  
 Subsequent doses 0.5 gram at 4 hour intervals for 4 days  
 Total dose 13.5 grams in 4 days

Colebrook also states that sulfapyridine is more effective in gas gangrene than sulfanilamide. The danger of granulocytopenia in the case of either drug is mentioned.

Delayed closure (11, 14, 40, 41, 43, 68) is recommended in wounds that are more than 12 hours old and, in the presence of obvious infection, they are thoroughly opened and irrigated with Dakin's solution. An electro-surgical apparatus weighing only 19 pounds has been designed for use in the recent Spanish War (8). Its use is enthusiastically advocated because the current destroys bacteria, bleeding is minimal, and postoperative shock is minimal presumably due to severed nerve ends and reduction in loss of blood. It is also suggested that roentgen-ray units be incorporated in the equipment of mobile surgical and evacuation hospitals for therapeutic use in all potentially dirty wounds (38). However, no evidence is given that the prophylactic use of roentgen-ray is beneficial as an ad-

junct to thorough débridement. Recent communications from Paris (27) reveal that the sulfanilamide derivatives are being applied to wounds *in situ* as a prophylactic measure. A Tudor Hart, a major in the Republican Army in the recent Spanish War, states that sulfanilamide was used in the treatment of septic wounds in Barcelona but the record of the results was lost when the city was captured with disorganization of the entire medical service (35).

**Compound fractures** Joseph Trueta, from his experience in the Spanish Republican Army has reported upon a total of 1,073 compound fractures treated by the "closed" method. This uniform method, consisting of immediate débridement after reduction of the fracture and immobilization in a plaster cast, in his experience, has proved of special value in wartime. This is particularly evident in that there were only 6 deaths in this series and only 1 case of gas gangrene. Some 20,000 cases were treated by this method, but detailed statistics are not available. This method of treatment which was advocated by H. Winnett Orr was employed over 30 months of continual treatment of war casualties, including the immediate surgical treatment of casualties in over 300 air raids. Although there was only one case of gas gangrene in the series of Trueta, one whole hospital in Madrid was utilized for the treatment of gas gangrene in General Franco's Army. Alvarez (65) in Madrid reports 61 cases coming under his care alone, and this complication was common enough that frequent appeals for large amounts of gas gangrene serum were made. It is significant that both armies were fighting on the same type of soil. A. D. Wall, in discussing the care of the wounded in the war in China in 1937, mentions that the closed treatment of compound fractures was utilized universally with excellent results. D'Harcourt, Folch and Oriol have published results from the application of this technique in the Republican Army. During the latter period of the war they were responsible for the treatment of 7,500 fractures and cared for 17,000 others treated in other centers. Although the total number of casualties is not available, in the Battle of the Ebro, for instance, a surgical unit dealt with 120

casualties, and in only 5 cases were amputations necessary. At the Valcarlos Hospital, Barcelona, of 5,000 wounded treated by them in 1 year only 26 secondary amputations were performed, and very few serious complications were encountered. In the course of the year the number of deaths among the 5,000 wounded was 37. 15 of these were due to gas gangrene, 17 were due to septicemia, and 5 to secondary hemorrhage.

It is emphasized that the essential procedure in the "closed" treatment of compound fractures is one of débridement, and Trueta feels that the factor of vitality of tissues as the decisive element in infections has not been given its due importance. The greatest danger of infection lies in devitalized muscle. The other great factor as pointed out by Ogilvie, is the length of time elapsing until treatment is instituted. Shock has been observed only in those cases in which there is delay in treatment which Trueta attributes in each instance to the absorption of devitalized muscle. The important principle in this treatment consists of (1) extensive and accurate débridement with removal of all foreign matter (2) reduction of the fracture—internal fixation is seldom used (3) after reduction, immobilization is accomplished with plaster which is virtually skin tight. The only padding used is for the os calcis, malleoli, and other bony prominences. The use of windows in the cast is vituperatively condemned as an avenue for the introduction of infection. Brewers yeast in the wound is recommended as a method of reducing the odorous qualities which are always present in a high degree.

The only failures of this method are attributed by the author to faulty technique which is usually inadequate débridement. Only 8 cases of lymphangitis or cellulitis were encountered in Trueta's series of 1,073. The final results as given in the *Lancet* (64) from the standpoint of function, are good, 90.9 per cent. bad 8.6 per cent. deaths, 0.5 per cent. To those who were engaged in the care of the wounded in the last war these figures are impressive.

However there are several articles in the French literature by those who received many of the Spanish refugees after the "closed"

method of treatment had been carried out. It is evident from their experiences that there may be pitfalls in this method (1:56-60).

Ricard, Francillon Deplante and Mathevon concluded from their experience in treating "many" of these refugees that many of the fractures were badly or not at all reduced, projectiles were often still present in the wound, and the infection present precluded the possibility of subsequent surgical treatment for months. Some of the wounds were apparently treated with superficial cleansing and immobilization alone. They felt, therefore that rigorous immobilization gave advantage only when proper treatment to the fracture had been carried out. They were likewise surprised to see the method applied to all cases, especially joints. Although, in general, the refugees were in good condition physically the condition of the extremity from the standpoint of function was extremely poor. This paper which was given at Lyon was then discussed by Peycelon who stated that he had occasion to treat 60 refugees, some wounds over 3 months old. He called attention to the fact that the Spaniards referred to this treatment as the "American method." Fistulas draining pus sometimes at a good distance from the original wound were observed in many instances. Others had extensive pressure areas in the axilla, on the palmar surface of the wrist with gangrene of the flexor tendons, ulcers over the popliteal space and over the malleoli. Five amputations of the thigh or arm were carried out because of the extensive infections. He therefore removed all plaster from these patients with remarkable improvement."

Mallet and Guy treated 83 Spanish casualties. Of this group 29 were immobilized in extensive plaster, 25 were fractures, and 4 extensive wounds of the soft tissues. Eleven had high temperatures. One amputation of the thigh was necessary because of the presence of infection.

The wounds encountered by Creyssel all seemed to be stagnant and the pressure areas sometimes assumed greater proportions than the original wounds. The plaster was badly applied and several of the patients had oscillating temperatures and chills. One thigh amputa-

tion had to be done. All of the complications were observed, however, in those patients in whom the initial removal of the foreign body had not been done. He concluded "The initial surgical act is indispensable and the cast should always be fenestrated."

Gabrielle treated 300 Spanish refugees in the Lyon hospital. One hundred were discharged immediately because of minor wounds. About *one-third* were found to have been treated correctly with good results. Sixty of these patients had not been operated upon at all, 40 were treated with simple dressings, and 20 were immobilized in circular plaster. The plaster which had been applied in the 10 cases of soft tissue injuries alone appeared useless, the joints were unnecessarily stiffened and the projectiles remained. He concludes "All casualties should be operated upon as soon as possible. It is useless to immobilize for transportation common wounds of soft tissue. Fractures should be correctly immobilized. In the French Army all fractures will be treated with good immobilization after operative treatment. The casts will be fenestrated for *surveillance* rather than for frequent dressings."

In the course of a detail early in 1939, Arnaud, Perves, Caire, and Morvon took care of more than 2,000 wounded militiamen of the Spanish War on the hospital ships *Marechal-Lyautey* and *Asni* (1). They observed about 600 cases of wounds of the extremities treated without exception by large circular closed plasters which had been applied over the fresh wounds. These wounded were received at the time of the complete debacle of the Republican Army. An interesting account follows:

"The wounded, forced from the surgical ambulances by the thrust of the victorious armies, had fled, and as best they could by their own means had crossed mountains covered with snow. Provided with thick plaster casts, reinforced and supported by splints with stirrup bandages to ease their walking, these wounded having had no attention for several days, badly nourished and sleeping in the open air, were collected and hospitalized on hospital ships. It was only the *survivors* of such exodus that we had under treatment. Most of the wounded had been struck by shell fragments, generally of small volume as were at least those pieces which were still in place and needed operation. These treatments seemed to us to have been made sometimes by improvised surgeons. On opening the plasters, we noticed without

difficulty not only that many of the wounds had been incompletely operated upon, since they still contained shell fragments but besides that the segments of the limbs were not always in the position allowing the best recuperation, especially in cases affecting the forearm and the wrist. The plaster casings gave off a fetid odor and in some cases we noted that a flow of pus appeared at one of the extremities of the plaster. Very few complained of having suffered in the course of their exodus or of suffering from lesions which their plaster cast concealed."

Extensive infections with fistulas were observed in certain instances. In 1 case, a compound fracture of the forearm was complicated by fistulas in the skin of the hand and forearm. Another fistulous tract ran from the base of the arm to the posterior part of the thorax. They noted almost without exception that these complications developed in unusual clinical silence for they were not accompanied by changes in temperature. About half of those who had a correct surgical operation at the time of injury had healed in the normal time and in an acceptable manner, although the neighboring soft tissues had not healed. The other half presented frankly mediocre results. As for the fractures of the femur, *all had bad results*. Secondary displacement had occurred under the plaster and angulation and overriding in the presence of infection constituted a complex orthopedic problem. The worst results were in joint wounds. They demanded amputation. The functional results were very mediocre and it appeared evident that the surgeon had shown little interest whatever in the possibility of functional recovery. Ankylosis in very bad positions, stiffness in many joints, vasomotor and cutaneous and bone changes, fingers held rigidly straight, were current observations as soon as the plaster was removed. Arnaud and his associates conclude that this method of treatment should be reserved only under unusual war conditions, namely, a great mass of wounded, or when there is difficulty in evacuation, reduced trained personnel, lack of dressings, etc.

"We consider it well established that the removal of the plasters should be as soon as possible after evacuation. Difficulty of inspection of the wounds under plaster is great and we cannot forget the separation of fractures, the arthritis that we have discovered after the removal of plasters, which no revealing symptom allowed us to suspect."



It is obvious that the unusual conditions occurring at the time of the debacle of the Republican Army have precluded a satisfactory analysis of the end results in these patients. A. Tudor Hart stresses the principle of continuity of treatment and of surgical responsibility in all cases. This can be achieved only if the patient is kept at one place. It is also recommended that there be standardization of stretchers so that a wounded person may not be moved from his original stretcher until the operating room is reached.

When these principles were observed, it was apparent that excellent results were obtained, however. Dr. Rudolph Matas (14) personally visited the Catalan war zone where over 5,000 wounded were under treatment. In one base hospital at Banolas, one ward devoted exclusively to fractured femurs had 75 or more patients under treatment. He states that there was apparent universal agreement on *dibride ment* reduction under mechanical traction and anesthesia, controlled by roentgenograms, with packing of the wound free drainage into a completely closed and immobilizing plaster encasement, which was allowed to remain *in situ* without change until the healing of the wound had advanced sufficiently to become protected by granulation against secondary infection.

#### Matas relates

I had an opportunity to see several plaster encasements removed from arms and thighs after they had been *in situ* for from 5 to 21 days. The stretch of the soiled encasement was nauseating. A magma or mush of decomposing pus, wound secretions, including sweat and other matter covered the surface of the wound under the plaster bandage. But after wiping this off with warm water and soap and when the pads were removed, I was surprised to see the excellent healthy pink, well-granulated appearance of the wounds coupled with a very satisfactory condition of the patients—no fever, no pain, good appetite, etc. This was indeed a revelation which I had not anticipated. Suffice it to say that when fresh wounds are relieved of all dead or devitalized tissues, they are when put to complete rest, quite able to take care of themselves without the aid of antiseptics, which hinder the normal reproduction of the tissue cells and weaken their defenses. At any rate it would seem that symbiotic existence is possible between the normal tissue cells and the saprophytic bacteria and other pathogenic organisms that gather under cover of plaster encasement. In fact if there was one essential for the successful treatment of frac-

tures, it was plaster of Paris. By the close of the war plaster had risen to the level of an apothecary in surgical esteem.

A statistical summary furnished by Jimeno (14) of Barcelona showed that 500 fractures of the femur had been treated by the "closed" method with a mortality of 16 or 3.2 per cent. There were 5 amputations—4 necessitated by infection and 1 by gas gangrene which had appeared before patients were admitted to the hospital.

A final opinion on this method of treating war wounded should probably be reserved. The results are equivocal inasmuch as on one hand one reads

"plaster had risen to the level of an apothecary in surgical esteem,

revelation which I had not anticipated.

"the plaster maintains a constant beneficial effect on the wound.

And on the other hand one reads

"pressure areas sometimes assumed greater proportions than the original wounds.

"Serous draining pus sometimes at a good distance from the wound."

a flow of pus appeared at one of the extremities of the plaster

as 1 of fractures of the femur all had bad results.

"functional results were very mediocre.

**Cranial wounds.** The incidence of cranial wounds in the French Army has dropped from 15 to 3 per cent since the introduction and use of a steel helmet (40). An excessive mortality rate in this group is attributed to primary hemorrhage so that only about 25 per cent reach the field hospital. Another great factor is the delay in transportation which necessarily increases the danger of intracranial infection. All treatment is concerned with prevention of infection and reduction of eventual cerebral phenomena. Sulfanilamide is employed freely and the necessity of skilled attention is stressed in this group of patients by the Germans (9). The German Army strives to treat all wounded within 8 hours, often flying the wounded soldier to the interior where trained personnel is available (62). The principles of traumatic neurosurgery during peace time are applicable in times of war. The greatest problem in times of war is the provision of adequate skilled personnel.

This need for specialized personnel is further evident in recent communications from London (30, 34). The London correspondent of the *Journal of The American Medical Association* writes that one of the latest advances in the British Army is a mobile unit for cranial surgery at the front. They have constructed a motor lorry which carries a separate engine and dynamo for cautery, lights, suction, and a 12 volt accumulator for an electromagnet. This unit carries two complete sets of neurosurgical instruments, two folding operating tables with head rests, two folding instrument tables, and anesthesia apparatus. There are also oil stoves for sterilizing. The Personnel includes 1 neurosurgeon, 1 neurologist, an anesthetist, 2 surgical assistants, and 2 operating-room nurses. This unit operates at casualty clearing stations and carries enough supplies for several hundred neurosurgical operations and may remain in the forward areas for weeks at a time. Units of this type answer the needs for medical care which may keep pace with the rapidly moving front.

The prevention of hemorrhage in extensive wounds of the face and oral cavity is accomplished by massive packing of the pharyngeal cavity followed by tracheotomy. The Japanese have employed this procedure on a large scale and are said to have saved many lives who would otherwise have died from hemorrhage at the field (17, 68).

*Thoracic wounds* Crafoord has estimated that 30 to 40 percent of all fatalities are due to chest injuries. Transportation of this group is especially dangerous and most of them die at the front from hemorrhage. The emergency nature of this type of wound should probably give it preference over all others (15, 33, 55). Ranson relates his experiences with gunshot wounds of the chest in the Sino-Japanese War during 1937. About 1 wound in every 12 is in the chest and the number of men who die on the field of chest wounds is from one-half to one-third of the total number killed. The English in the war of the Crimea lost 79.2 per cent of all men who were wounded in the chest and who arrived at the hospitals for treatment. The figures then show a definite progress and trend through the American

Civil War, the Franco-Prussian War, the Spanish-American War, the Boer War, the World War, and the Sino-Japanese War of 1937. In the last war, the wounded who died from chest wounds after being treated in the hospital amounted to only 14.8 per cent.

Pneumothorax is a most important consideration in the treatment of chest wounds. Mediastinal flutter is of great importance because of its effect upon the great veins which carry blood to the heart. The systolic output is dependent upon the diastolic inflow, and the mediastinal flutter causes periodic obstruction to both the superior and inferior venæ cavæ. The symptoms of open pneumothorax are due, therefore, to a circulatory disturbance rather than to the respiratory disturbance *per se*. Other important points are the rapid loss of heat from the chest and the great tendency toward infection. Tension pneumothorax produces even more marked symptoms of distress than the open variety because the pressure in the pleural cavity of both sides approaches a positive value. A tension pneumothorax, unless relieved, invariably leads to a fatal outcome.

The carefully managed differential pressure treatment as carried out by Sauerbruch in the World War resulted in only an 18 per cent mortality in 300 cases. The use of heavy dressings which restrict thoracic breathing is warned against. The treatment consists of thorough débridement, resection of ribs with a good opening into the pleural cavity. The pleural cavity is carefully cleansed and all vessels which are bleeding are ligated, foreign bodies are extracted, and débridement of injuries to the lung is carried out with primary suture. Lobectomy or pneumonectomy may be indicated. Exact suture of tracheal or extrapulmonary bronchial injuries is carried out and the esophagus is carefully examined for injuries. Primary suture of the defects in the chest wall follows closure of the parietal pleura after the lung is expanded. Crafoord classifies thoracic wounds as (1) wide open pneumothorax, (2) outer or inner bleeding, (3) tension pneumothorax, (4) mediastinal emphysema, and (5) injuries to the esophagus.

*Abdominal wounds* A war of motion causes a greater incidence of abdominal wounds. In

1917-1918 in the Finnish War the incidence was only 2.97 per cent in the World War 4.6 per cent (63). During the World War surgical operation was regularly employed. Prognosis during the first 6 to 8 hours was excellent and later than 36 hours the mortality rate approached 100 per cent. Matas (61) in discussing penetrating wounds of the abdomen quotes Baron who has estimated that 10 per cent of the 1,185,000 soldiers who were killed outright on the battle field in the World War died from the shock and hemorrhage of penetrating abdominal wounds. Therefore, 118,500 abdominal deaths on the battle-field occurred before any surgical assistance could possibly reach the stricken men. Death follows gunshot and other wounds of the abdomen as a result of hemorrhage, shock, and infection. Although shock and hemorrhage require prompt institution of measures at the front, it is possible that infection following abdominal wounds can be greatly minimized. Storck outlines investigations that are now being done to determine the possibility of replacing the pathogenic bacteria with non-pathogenic ones in the intestinal tract of soldiers before going into battle. By feeding cultures of *Bacillus acidophilus* for 3 or 4 days it is possible to change the bacterial flora of the intestinal tract, and it is hoped by this means that infection following war abdominal injuries can be greatly reduced.

The principles of peace-time abdominal surgery are perfectly valid in times of war. Cases should be carefully selected with localization of foreign bodies by x-ray along with institution of pre-operative measures to combat shock. Little is accomplished in any event by laparotomy after 12 hours with the possible exception of prolonged hemorrhage from upper abdominal wounds. Pre-operative measures include heat, morphine, 100 per cent oxygen for air-hunger, blood in adequate amounts and 3000 units of antitoxin. Blood has become generally available through improvements in preservation, refrigeration and transportation (10-20-22-26-51-58). Spinal anesthesia is used cautiously. Ether is used frequently because of its general availability.

Matas provides a bibliography of recent Spanish War literature on abdominal wounds (2-6-12-16-19, 59). He summarized them as follows:

"The general conclusions arrived at by Baron (2-3) serve as a sample of the general surgical experience of the Spanish Civil War. Of 500 well recorded abdominal wounds, 39, or 47 per cent, are regarded as inoperable and were not celiotomized because (1) they were brought from the field in hopeless, dying condition—(a) this group there are 9 of the wounded of whom 97 per cent died. (b) in 47 of the non-operated upon group celiotomies are performed because the visceral lesions are limited to the liver and it was thought that they had better chance of survival without operation. The mortality in this group was 90 per cent, thereby confirming the good judgment of the surgeons in not operating. (2) Celiotomies were performed for penetrating gunshot wounds in 26 patients (5 per cent of the 500 divisions) on an average of 7.5 hours after the injury had been inflicted. In all of these celiotomized patients the lesions involved, almost exclusively the parenchymatous organs, especially the liver and, in this group there are 47 recoveries, or a mortality of 54 per cent. (3) Three hundred forty were celiotomized for lesions of the gastro-intestinal tract, alone or conjointly with their visceral wounds. In this group only 5 per cent recovered and 75 per cent died. (4) Not included in these 500 cases were 22 exploratory celiotomies for penetrating and non-penetrating, uncomplicated visceral injuries the mortality in this group was 55 per cent. In addition, there were 6 patients with possibly penetrating but seemingly uncomplicated wounds. In this group the mortality was only 6 per cent. (5) The great increase in military warfare, machine guns, explosive shells, shrapnel, hand grenades, aerial bombs, trench mortars, etc., has increased the mortality of the abdominal wounds by their multiplicity and wider range of destructive action and complications. (6) The number of fatally wounded who survived long enough from the shock and hemorrhage on the battle-field to reach the casualty stations in a moribund and hopeless condition is increasing (35-47 per cent). This is particularly characteristic of trench warfare, when the fatally wounded patients die on the field if delayed in transportation but survive just long enough to expire in the field hospitals when the distance is short and the stretcher bearers are promptly on the spot. (7) Despite the best care and skill, the mortality of exploratory celiotomies is still high, 37 per cent. (8) It would seem that, despite the free and abundant resort to transfusion with whole or preserved blood, and despite favorable conditions for operation, the mortality in performing wounds of the gastro-intestinal tract still remains high, 75 per cent. (9) The mortality of gunshot wounds of the abdomen involving the gastro-intestinal tract shows relatively little improvement over

the mortality of the same wounds recorded in the experience of the allied French, British and American surgeons or of German operators at the close of the World War, which was largely a stabilized trench war with surgical dugouts close by (10) Undoubtedly, exposure in freezing temperatures, delay in transportation, starvation, hasty mobilization of the surgical staff, and patients in mobile wars exercise a very decided influence upon the prognosis, all of which was well exemplified in the freezing winter temperatures at Teruel, the Ebro, Segre, and Pyrenean slopes "

*Transportation* The ultimate outcome of a wounded soldier depends largely on the time interval which elapses before effective treatment is instituted Meningitis, peritonitis, and pneumonia are sequels of delay in treatment of cranial, abdominal, and thoracic wounds, which may increase mortality rates tenfold The ambulance plane coping with problems accompanying increased mobility of the front has made it possible to provide for the wounded the highly developed surgical facilities of the home hospitals W Toennis of the German Air Force relates experiences in the Polish campaign Transportation of 2,500 wounded from Poland to Germany was accomplished by air-transport without undue difficulty Those with marked secondary anemia were susceptible to "airsickness," which was best relieved by the administration of oxygen The breathing capacity which is reduced in gunshot wounds of the chest with hemothorax, and in abdominal wounds with elevation of the diaphragm, demands special precautions in transportation Respiratory difficulty was observed in these patients at 1,300 meters and was relieved promptly by the administration of oxygen Of 2,500 wounded and sick, transported by plane, only 4 died during the flight or immediately upon landing Three of the cases mentioned had peritonitis It was noted that all deaths in flight occurred in planes *not equipped with oxygen* In a comparison of air transport with land, it is beyond doubt that the former method is less painful, first because of the short duration and second because few jolts are sustained

A soldier with prolapse of the small intestine, the result of an abdominal shot wound received while in the vicinity of Warsaw,

reached the operating table in the clinic at the University of Breslau 2½ hours after he was wounded, the actual time of flight being 90 minutes Thanks to this record speed the wounded man recovered without complications The same applied to wounds of the jaw and brain, for the treatment of which, in the field there were neither facilities nor personnel at hand The majority of patients with head injuries operated upon at the front where no knowledge existed as to the extent of comminuted fractures were not lucky enough to be transported promptly into the indicated section of the home hospitals, and died of cerebral abscesses By contrast, the patients who were not operated upon and could be observed in the airbase hospital of Berlin, after final treatment, showed no infection Among the 10 patients taken to the hospital by plane, there were 3 with infection caused by hemolytic streptococci All such patients transported by air may look forward to recovery Quick and careful air transportation brought 39 patients with wounds in a short time to a place where they could receive extensive treatment, and where they had absolute quiet Only 2 of the patients died weeks later from empyema

"When comparing these results with those of the World War, we who served there and are serving now, have no doubt of the progress made when we can say that of 375 joint-shot fractures treated, but 2 died," (62)

*Prevention of war wounds* The value of physical prophylaxis of wounds is apparent from the fact that cranial wounds have been reduced from an incidence of 15 to 3 per cent since the introduction of the steel helmet It is significant that the great majority of wounds are caused by small missiles of low velocity Although the armor necessary to protect against high velocity bullets may weigh as much as 20 pounds, compressed fiber or bakelite panels (with the same tensile strength as aluminum and one-half the weight) will suffice for protection against shrapnel and trench-mortar splinters It is logically assumed that many chest and abdominal wounds, which in the past have been caused by low velocity missiles, may be prevented by the use of some form of light weight body armor

Sauerbruch found 37 per cent of those dead on the battle field had extensive chest wounds while at the casualty clearing station the percentage was only 3 (29). Thus in the trenches the vast majority of chest wounds prove fatal from hemorrhage. The recognition by the Germans of the value of preventing wounds in this manner has led to unsuccessful attempts by the Hitler régime to induce an American inventor of armor to equip the German armies (32). However a war correspondent now reports that the Germans are regularly employing some type of body armor.

Sir Richard Cruick (31) ophthalmologist, has devised a 22 gauge retractible duralumin visor as an accessory to the helmet already in use. He estimates that from 50 to 70 per cent of the blindness which in the last war was caused by small missiles may be prevented in this manner.

Sir Harold Gillies has suggested a gauntlet to protect the back of the hand (33). Mr Kenneth Walker advocates a light armor for the chest which may also be used as an entrenching instrument with a supplied handle. Interest in the subject of armor in England was highly apparent at a recent meeting of the Royal Society of Medicine where a discussion took place on "the physical prophylaxis of wounds." The following resolutions were unanimously adopted:

"That this representative meeting of the Royal Society of Medicine, after full discussion of the question, is emphatically of the opinion that the physical protection of the members of the fighting forces on and should be improved by closer collaboration between the medical profession and the appropriate technical experts of the Admiralty, W. Office and Air Ministry.

That this meeting of the Royal Society of Medicine resolves that the Council be asked to consider the formation of a special committee to this end. As the matter is one of extreme urgency and importance it is hoped that the president may use his emergency powers and approach the government with the offer of the society's co-operation at the earliest possible date.

#### SUMMARY AND CONCLUSIONS

The incomplete reports of surgeons caring for the wounded in the present wars indicate more than ever the importance of a sound knowledge of the fundamentals of surgery.

Careful débridement skillfully carried out is still the one most important treatment for wounds. Without it no supplementary form of treatment will succeed. Chemotherapy may become important but there is need for more investigation before its utility becomes firmly established. The value of physical prophylaxis of wounds should be vigorously investigated especially as the majority of wounds are caused by the predominant low velocity missile. The value of mobile operating units coping with the increased need for skilled personnel at the front, is recognized. The ambulance plane has already proved of inestimable value. Rapidity in the collection and transportation of wounded reduces the incidence of peritonitis, meningitis, and septicemia. Although conditions may be far from ideal, the principles of peace time surgery continue to be perfectly valid in times of war.

#### BIBLIOGRAPHY

1. ARNOLD, M., PERRY, J., CURRY, A. and MORSON, F. *Médecine Acad. de chir.* 930, 63, 80.
2. BAXON, A. G. *Rev. espan. de méd. y cirug. de guerra*, 930, 5, 3.
3. *Ibid.*, 36.
4. *Ibid.*, 930, 3, 73.
5. BASTON, M. *Rev. de méd. de guerre*, 935.
6. BENDON, R. F. *Rev. de méd. de guerre*, 935, 24.
7. BILBAO ROJAS, D. *Médecine Acad. de chir.* 937, 63, 71.
8. BLANCH, G. M. *Mil. Surgeon*, 930, 84, 377.
9. BUCKHA, A. *Wien. Klin. Wochenschr.* 930, 3, 80.
10. BUCHHEITEL DE LA CAMP, H. *Deutsche Zeitschr. f. Chir.* 930, 3, 366.
11. BUCHHEITEL, St. J. *D. Brit. M. J.* 930, 241, 304.
12. CAYTO BORRERO, N. *Rev. espan. de méd. y cirug. de guerra*, 930.
13. CHALTON, M. K. *Mil. Surgeon*, 930, 85, 20.
14. COLLIER, F. A. and VALL, W. L. *Ann. Surg.* 940, 50.
15. CRAWFORD, C. *Nord. méd.* 930, 3, 1729.
16. CENDRADO F. *Rev. espan. de méd. y cirug. de guerra*, 930, 3, 267.
17. DERRON, J. *Rev. de laryngol. etc.* 930, 60, 713.
18. D'HAMOUR, J., FOLCH, A. and OROSC, A. *Brit. M. J.* 940, 65.
19. DUBON, G. *Rev. espan. de méd. y cirug. de guerra*, 930, 3, 8.
20. EDWARDS, F. R. K. A. J. and D. H. T. B. *Brit. M. J.* 940, 377.
21. FIEBIGER, A. *Schweiz. med. Wochenschr.* 930, 80, 347.
22. Foreign letters. *J. Am. M. Ass.* 940, 4, 569.
23. *Ibid.*, p. 68.
24. *Ibid.*, p. 7.
25. *Ibid.*, p. 304.
26. *Ibid.*, p. 4.
27. *Ibid.*, p. 904.
28. *Ibid.*, p. 683.
29. *Ibid.*, p. 8041.
30. *Ibid.*, p. 14.
31. *Ibid.*, p. 397.

- 32 Ibid 115 626
- 33 GASK, G E Brit M J, 1939, 1 1043
- 34 Great Britain Ministry of Health, 1940, memo no 4
- 35 HART, A T Brit M J, 1939, 1 1099, 1146
- 36 HOTTEN, W I T Med J Australia, 1940, 1 132
- 37 JEANNENEY Gaz d hôp, 1939, 112 1437
- 38 KEATING, P M, and DAVIS, F M Mil. Surgeon, 1940, 86 235
- 39 LASHER, W W Mil. Surgeon, 1940, 86 162
- 40 LAUWERS, E Presse méd, 1940, 48 32
- 41 LERICHE, R Presse méd, 1940, 48 1
- 42 LOCKWOOD, A L Brit. M J, 1940, 1 456, 401, 445, 494.
- 43 LYLE, H. H. M Mil. Surgeon, 1939, 84 580
- 44 METER, E J Schweiz med Wchnschr, 1940, 70 37
- 45 OGILVIE, W H Brit. M J, 1938, 1 132 and 183
- 46 ORR, H W J Am M Ass, 1922, 79 255
- 47 Idem Surg, Gynec. & Obst., 1927, 45 446
- 48 Idem Osteomyelitis and Compound Fractures St Louis C V Mosby, 1929
- 49 Idem A New Era in Treatment of Osteomyelitis and Other Infections St Paul Bruce Pub Co, 1930
- 50 Idem Arch Surg, 1940, 40 825
- 51 DE LA PENA REGIDOR Schweiz med Wchnschr, 1939, 69 682
- 52 PARKINSON, C K Med J Australia, 1940, 1 94
- 53 PARROTT, A H Proc. Roy Soc Med, 1938, 32 53
- 54 PERMAN, E Nord méd, 1939, 3 2435
- 55 RANSON, F T J Thoracic Surg, 1940, 9 278
- 56 RICARD, FANCILLON, DEPLANTE, and MATHENON Lyon chir, 1940, 36 573
- 57 SCHOENE, G Zentralbl f Chir, 1938, 65 1137
- 58 SCHUBERT, O Nord méd, 1939, 3 2442
- 59 SEVILLA, C R Rev espan de méd y cirug de guerra, 1939, 3 66
- 60 SOULIE, J, and LINARES, C J de chir, 1940, 55 22
- 61 STORCK, A H Ann Surg, 1940, 111 775
- 62 TOENNIS, W Mil Surgeon, 1940, 87 22
- 63 TROELL, A Nord méd, 1939, 3 2724
- 64 TRUETA, J Lancet, 1939, 1 1452
- 65 Idem Proc. Roy Soc Med, 1939, 33 65
- 66 Idem Brit M J, 1939, 2 1073
- 67 Idem The Treatment of War Wounds and Fractures New York Paul B Hoeber, 1940
- 68 WEDDELL, I M Brit. M J, 1939, 1 785
- 69 WIEBECK, B H Zentralbl f Chir, 1938, 65 1043

# RATIONALE AND USE OF OXYGEN IN THE POSTOPERATIVE TREATMENT OF HYPERTHYROIDISM

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**O**X YGEN is a valuable adjunct in the immediate postoperative treatment of patients with toxic goiter. A few reports of its use are found in the literature. Haunes and Boothby report its value in 91 patients having severe reactions and cyanosis after thyroidectomy. Schmidt has employed oxygen therapy immediately after thyroidectomy and other surgical procedures with beneficial results. Maddock also comments upon the efficacy of oxygen in the treatment of patients following thyroidectomy. The use of oxygen therapy, however is not as extensive as it should be, chiefly because of lack of understanding of its rôle in maintaining homeostasis and lack of understanding of the increased oxygen requirements of the hyperthyroid patient.

It should be kept in mind that anoxemia is present long before cyanosis becomes visible. This is most important in the toxic hyperthyroid patient whose oxygen requirements are greater than those of a normal patient and in whom cyanosis is of grave significance. In order to have cyanosis at least 5 gram per cent of reduced hemoglobin must be present. Of practical general significance is the fact that in severe anemia where the blood hemoglobin approaches 5 gram per cent, cyanosis does not develop until the patient is almost moribund below 5 gram per cent cyanosis cannot occur.

The literature contains a report which indicates that arterial blood oxygen saturation may be decreased below normal in patients with hyperthyroidism. Lataczek reports decreased arterial blood oxygen saturation in 2 of 3 patients with elevated basal metabolic rates (plus 52 to plus 56). We have also determined the femoral artery blood oxygen saturation in 12 hyperthyroid patients before and about 1 hour after thyroidectomy. The

samples of femoral artery blood were obtained anaerobically and assayed for oxygen saturation according to the method of Van Slyke and Neill. A record of the blood pressure, pulse, and respiration was also made. Table I shows that the normal oxygen saturation (average 92 per cent) was significantly depressed 2 to 7 per cent in 6 of the 12 patients under basal conditions before the operation. Depression of oxygen saturation was seen most frequently in toxic patients with high metabolic rates. Samples of blood were taken again about 1 hour after the operation. The operations were done under a basal anesthetic of avertin (70 to 90 milligrams per kilogram body weight) supplemented with ethylene and oxygen. The combination of avertin ethylene and oxygen caused less depression of arterial blood oxygen saturation than barbiturates, paraldehyde and nitrous oxide anesthesia reported elsewhere by us (9). However in spite of this, further depression of arterial blood oxygen saturation was observed following operation in 10 of the 12 patients. In Case 8 the oxygen saturation was depressed to 78.1 per cent. No significant fall in blood pressure was observed in any of these cases. Most of the patients developed a slightly elevated blood pressure pulse and respiratory rate after the operation. These studies are significant in so far as they revealed that some of the hyperthyroid patients had a mild under saturation of blood oxygen prior to operation and that this was worse after the anesthetic and operation. This degree of anoxemia is deleterious in view of the fact that there is an increased consumption and need for oxygen in the hyperthyroid patient. This has been shown experimentally in animals and also in our patients. By means of the Warburg gasometric apparatus Reinwein has found that the addition of thyroxin to the substrate increased the consumption of oxygen by liver





TABLE II.—RELATION OF BASAL METABOLIC RATE TO VITAL PROCESSES AND ABSORPTION OF OXYGEN

Patient	Hypothyroid		Normal		Hyperthyroid					
	B.M.R.	C.O. <sub>2</sub> in per min.	B.M.R.	C.O. <sub>2</sub> in per min.	B.M.R.	C.O. <sub>2</sub> in per min.	B.M.R.	C.O. <sub>2</sub> in per min.	B.M.R.	C.O. <sub>2</sub> in per min.
	-13	54	—	—	+36	93	+54	106	+71	106
	-4	56	±	—	+2	75	+36	979	+73	105
2.	—	166	+	7	+25	129	+3	66	+64	300
4.	-13	57	±	51	+25	130	+34	36	+64	107
	-22	58	±	92	+20	96	+11	96	+64	106
6	-5	154	±	100	+41	205	+11	—	+7	106
	—	154	+	100	+41	254	+13	107	+6	101
8.	-67	144	±	96	+	100	+11	106	+64	113
	-66	151	+6	171	+3	106	+1	100	+77	100
10.	-75	59	+3	100	+36	104	+17	107	+68	111
C.O. <sub>2</sub> in Absorbed	-20 to -30	57 cm	-4 to +4	114	Average		+35 to +41	10	+55 to +70	106
T (°F)		97		98				98		98.6
P		70		70		24.6		98.6		1.4
		1		17		18.7		10		4

output greatly decreases the cardiac reserve. The increased pulse rate interferes with the coronary circulation to the myocardium because of the shortened diastole during which phase filling of the coronary vessels occurs. Prolonged anoxemia under increased demand may lead to angina pectoris, coronary occlusion, myocardial asthenia, and decompensation. The hyperexcitability of the nervous system may lead to arrhythmia and irregularity. Acute and chronic anoxemia causes enlargement (Van Lier) hypertrophy (Bouchut) and fatty degeneration (Hiltzenberger) of the heart.

With an increased basal metabolic rate there occurred an increase in the respiratory rate. The tachypnea is a physiological attempt to increase the absorption of oxygen and to facilitate aeration of the quickened circulation. Dyspnea is a prominent symptom in advanced cases. The irritable patient with a toxic goiter is conscious of this difficulty in breathing and feels that he must voluntarily assist the normal movements. This leads to increased restlessness and nervousness. The dyspnea may be (1) reflex from worry, restlessness, sleeplessness, (2) cardiac insufficiency, and (3) decreased vital capacity. In hyperthyroid patients the vital capacity is

decreased below normal (3700 cubic centimeters) due to increased tone together with some inco-ordination of the skeletal muscles and an increased irritability of the vagus nerve endings in the lungs. Asher (1) has demonstrated the effect of the thyroid gland upon sensitivity to anoxia. Rats fed thyroid extract showed signs of air hunger and suffocation in atmospheres the oxygen deficiency of which did not affect normal rats. He also reported (2) that rats whose thyroid glands have been removed did not show any of the phenomena of suffocation exhibited by normal rats in oxygen deficient atmospheres.

Physiological processes are less stable than in the normal patient and therefore the reactions of the toxic thyroid patient should be closely watched because they are violent and superimpose a further strain upon the already overburdened vital reserves. An increase in the pulse rate may be one of the early signs of increased oxygen demand. Frequently this may become elevated to 130 to 160 beats per minute. The respiratory rate may increase to 40 or 50 respirations per minute and the body temperature may rise to 104 or 105 degrees F. These reactions are most common following thyroidectomy in the very toxic patient. How

# THE SURGICAL PROBLEM OF CHRONIC GASTRITIS

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THE early diagnosis of gastric carcinoma is the hope of every surgeon. Unfortunately, at surgical exploration, disappointments are all too common, even when the clinical symptoms seem relatively early. Gastroscopy now offers another aid in the early and differential diagnosis of malignancy (15, 18). Although no biopsy is possible by this method, it has stimulated a greater interest in the histopathology of the gastric mucosa, by correlating the gastroscopic picture with the microscopic study of surgical specimens. In the evaluation of this knowledge, however, cases occasionally occur that present great difficulty in the differential diagnosis of carcinoma from the chronic hyperplastic form of gastritis. These unusual cases may perplex not only the roentgenologist, but also the gastroscopist, and at times even the surgeon during exploration of the stomach. Unless the latter is familiar with this pathological condition, he may well be confused as to the proper policy to pursue when suddenly confronted with the situation during operation. We wish to discuss this problem, and to report a few cases in point.

The gastroscopic clinic at this hospital is in the hands of well trained men. It has functioned with increasing success for the past 3 years and has been of great value as a diagnostic aid. We state this advisedly, lest it be considered that the gastroscopic observations reported here were at fault. In addition, we quote similar experiences of men well versed in the method.

Two types of hyperplastic gastritis have been described which, when severe, may simulate tumor formation. Schindler (15) speaks of chronic hypertrophic gastritis as an entity, entirely benign but frequently more intractable to medical treatment than peptic ulcer. There is mucosal proliferation of varying degree, and cellular infiltration of lymphocytes and plasma cells, with superficial ulcerations often occurring. On the other hand, there is a

chronic hyperplastic form, usually described as an antral gastritis, characterized by atrophy of the glandular elements of the mucosa, but hyperplasia of the surface and crypt epithelium and connective tissue. This condition is believed to be probably precancerous (7, 10, 11, 17). In either condition, the cellular infiltration may extend to the muscularis mucosæ and the submucosa, and there may be submucosal and muscular hypertrophy. Faber suggests that both types may be different stages of a progressive disease, rather than distinct entities. A severe hyperplastic gastritis may give rise to symptoms that are confusing with those of ulcer, polyposis, carcinoma, and lymphoblastoma. There is nothing characteristic of the gastric acidity, and the stools may or may not show occult blood (15).

The senior author and Pearl (4) were the first to describe a case of hypertrophic gastritis simulating tumor formation, in a paper on polyposis, 1926. Although the history, symptoms, and roentgen findings pointed toward polyposis, at operation the surgeon was confronted with an entirely unexpected and unusual condition, which was difficult to classify at the time. We describe it here in some detail, since it is now known to fit into the category of the cases to be presented.

A woman, aged 30 years, had complained of indigestion, occasional vomiting, diarrhea, and upper abdominal pains for 10 years, growing progressively worse. Physical examination was negative. Laboratory examination revealed a mild secondary anemia, occult blood in the stools, and an achlorhydria. Roentgenological examination disclosed multiple small, finger-like filling defects along the upper two-thirds of the greater curvature, and to a lesser degree along the lesser curvature. A diagnosis was made of diffuse gastric polyposis. At operation, however, only a slight thickening of the stomach wall was felt. Through an anterior gastrotomy incision, no polyps were evident, but a markedly hypertrophied mucosa thrown into enormous folds of various sizes, some 7 to 9 centimeters high. This very thickened mucosa was freely movable upon the submucosa and could be actually withdrawn through the incision. The hypertrophy involved chiefly the proximal two-thirds of the greater curvature and the upper third

202 consecutive operations. This is a mortality of 2.4 per cent. Two of these deaths were due to bronchopneumonia the 3 others to acute hyperthyroidism. All of these patients were close to 60 years of age and had hypertensive heart disease. In addition, one of them had diabetes and arteriosclerotic kidney disease. Because of the number of varying factors such as better pre-operative preparation and stage operations, it is difficult to evaluate the rôle that oxygen therapy had in this reduced mortality rate. However we could not help but be impressed with certain features. The cool moist atmosphere in the liquid oxygen tent and the high oxygen concentration exerted a sedative action and decreased restlessness the high oxygen tension made breathing easier so that the rate decreased and dyspnea was less severe or abolished. It decreased the heart rate and so maintained the cardiac reserve frequently correcting arrhythmia and decompensation. Early restoration of the elevated post operative body temperature to normal was frequently seen. A typical reaction is seen in Figure 2. The increased availability of oxygen in the tent atmosphere (average 60 per cent oxygen) gave the toxic patients the subjective sensation of well being and objectively they did not appear as sick as one might have expected them to be.

#### SUMMARY

1. Six of 12 hyperthyroid patients under basal conditions showed a depression of arterial blood oxygen saturation 2 to 7 per cent below normal. About one hour after thyroidectomy performed under avertin ethylene and oxygen anesthesia, 10 of the 11 patients showed a further depression of oxygen saturation. In 1 patient the oxygen saturation was depressed to 78.1 per cent.

2. Under basal conditions progressive hyperthyroidism is associated with an increased consumption of oxygen. A group of hyper-

thyroid patients consumed 56 per cent more oxygen than a similar group of normal patients.

3. Vital processes, such as body temperature, pulse and respiratory rates, are increased above normal in patients with toxic goiter. This decreases the systemic and cardiac reserve.

4. An increasing pulse rate is frequently one of the first signs of increased demand and diminishing reserve.

5. Anoxemia is present long before cyanosis becomes visible.

6. Oxygen therapy is indicated in the post operative treatment of patients with toxic goiter because they showed a postoperative anoxemia and because they utilize more oxygen than the normal patient.

7. Oxygen therapy exerts a sedative effect upon the patient following thyroidectomy. It facilitates aeration in the lungs decreasing the respiratory rate and diminishing or abolishing dyspnea. The heart rate is slowed and prompt reductions in body temperature are seen.

8. Oxygen therapy better pre-operative preparation short interval stage operations, have all helped to decrease the mortality to 2.4 per cent in 202 consecutive operations for toxic goiter.

#### BIBLIOGRAPHY

1. ASKER and DORAN. *Biochem. Ztschr.* 920, 106. 34
2. ASKER and SCHROEDER. *Biochem. Ztschr.* 928, 87. 399
3. B. ELLI. *Surg. Gynec. & Obst.*, 934, 59. 41
4. BOCCACCIO, FRIEDRICH, and BOCCACCIO. *Lyon med.* 934, 33. 40
5. HARTMAN and BOOTHBY. *Am. J. Surg.* 930, 6
6. HINTERBERGER. *Med. Klin.* 935, 34. 304
7. LITACHEW, AUBERT, and COMTELESCO. *Compt. rend. Soc. de biol.*, 933, 84
8. MADDOCK. *J. Michigan State M. Soc.*, 939, 35. 403
9. McCURRY, HARTMAN, SCHROEDER and SCHILLING. *Ann. Surg.*, 939, 835
10. McGRAW. *Ann. Surg.* 938, 97. 98
11. REIDWITZ and SWOPE. *Biochem. Ztschr.* 928, 87. 34
12. SATO, TOMOKU. *J. Exper. Med.*, 933, 85
13. SCHROEDER. *J. Michigan State M. Soc.*, 939, 38. 409
14. SPENCE. *Brit. J. Exp. Path.* 938, 3. 149
15. VAN LEEUW. *Am. J. Physiol.* 937, 8. 737
16. V. S. VEE and NEILL. *J. Biol. Chem.* 926, 6. 53



Fig 1 Case 1 Roentgenogram, August 15, 1938, showing the multiple irregular filling defects in the lower two thirds of the stomach, suggestive of a polypoid neoplasm

pituitarism, hypogonadism and hypothyroidism. Definite epigastric tenderness was present. There was bilateral pitting edema of the lower legs.

Laboratory examination disclosed hemoglobin, 80 per cent, red cell count, 4,700,000, white cell count, 12,600. Wassermann and Kahn blood tests were negative. Patient refused a gastric analysis, but the vomitus showed an absence of free hydrochloric acid, and a total acidity of 7. Stools contained occult blood.

Roentgenological examinations by Dr L. Bryan showed the following. On August 15, 1938, the lower



Fig 2 Case 1 Photograph of the resected specimen before fixation, illustrating the marked mucosal hypertrophy and the tortuous, thickened, nodular folds

two thirds of the stomach presented irregular filling defects, with diminished peristalsis (Fig 1). A polypoid carcinoma was diagnosed, but the presence of a true polyposis or lymphoblastoma was also considered. Roentgen therapy was advised to rule out the presence of a lymphoblastoma. Re-examination 2 weeks later (August 26, 1938) revealed an increased number of multiple irregular defects extending from the pylorus almost to the cardia. A diffuse papillomatous tumor was diagnosed, showing no response

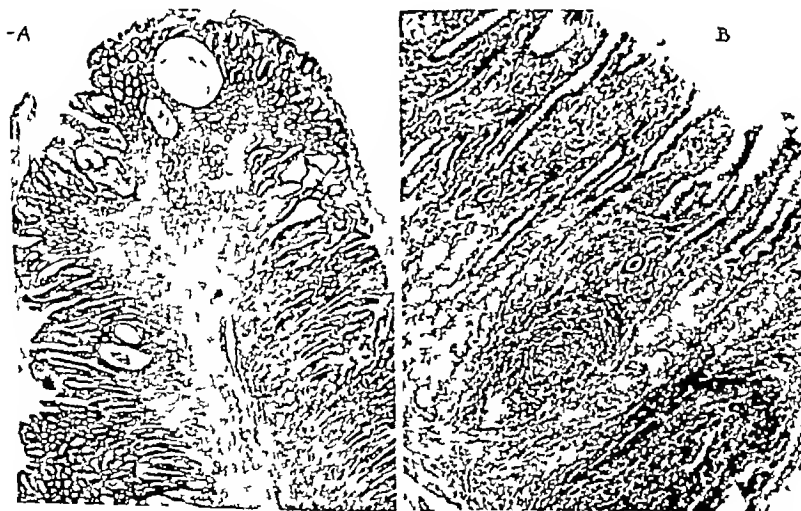


Fig 3 Case 1 a, left Section of an hypertrophied polypoid mucosal fold, with cystic and tortuous glandular alterations. b, Section of mucosa under higher power illustrating the extensive infiltration of plasma cells and lymphocytes, and the hypertrophied lymphoid follicles

of the lesser curvature merging gradually into the adjacent normal mucosa. Specimens were obtained at different sites, and the gastrotomy opening was closed after a large portion of prolapsed mucosa was removed. The patient made an uneventful recovery. Pathological examination by Dr Rusk revealed a distinct thickening of the mucosa, with normal surface epithelium. The surface presented occasional shallow clefts. The glands were very tortuous and lined with normal epithelium. Some of the glands in the deeper portion of the mucosa were dilated into small cysts. A marked edema involved the interstitial tissue of the mucosa, the muscularis mucosae, and the submucosa. This edema was associated with a marked infiltration of plasma cells, frequent eosinophils, and occasional large undifferentiated mononuclear cells, and extended in moderate degree through the muscularis mucosae. Frequent focal hemorrhages were scattered throughout the mucosa, with conspicuous dilatation of blood vessels throughout. Lymphoid follicles showed no abnormality. A pathological diagnosis of hypertrophic gastritis was made. After 4 years, intermittent attacks of mild abdominal distress and diarrhea still occur controlled fairly well by a bland diet and dilute hydrochloric acid.

Schundler (16) recently described several striking cases of proliferative gastritis, in which even at surgical exploration, as well as by roentgen and gastroscopic means, it was difficult to make a definite diagnosis. He included in his group Case 1 of this series, which is here described in full. In treatment, he advises resection only in isolated polypoid gastritis of the antrum, which is probably precancerous. When the diagnosis is uncertain as to hypertrophic gastritis or carcinoma, he favors thorough microscopic examination of a biopsy specimen with delay of resection until carcinoma is proved since frozen sections of the gastric wall are unsatisfactory. Otherwise, conservative treatment is recommended because of the hazards of gastrectomy.

Konjetzny (17) on the other hand, believes that resection is indicated in all these doubtful cases, since it not only furnishes the final diagnosis but also effects a cure. He reported 3 cases of tumor-like gastritis, entirely well 5 and 6 years after operation. Floercken has had similar results and agrees with Konjetzny as to therapy.

Kantor described 2 cases of giant rugae on the greater curvature of the stomach in which the roentgenological appearance suggested carcinoma. The presence of hypertrophic gastritis was disclosed at operation. Crohn re-

ported 8 similar cases, in 6 of which operation was performed under the diagnosis of malignancy. In addition, there were 9 cases of antral gastritis of marked degree, in 5 of which resection was done for carcinoma. Gastrosco-  
py was not available in these cases. Eusterman has described several similar cases at the Mayo Clinic.

Both Moutier and Benedict (13) also give testimony as to the gastroscopic difficulties in these conditions. They describe cases in which carcinoma was suspected but could not be definitely diagnosed, which eventually proved to be malignant, and cases in which carcinoma was thought to be present, but subsequently were found to be hyperplastic gastritis. This corresponds to our own experience. Benedict (1) concludes that exploratory operation is indicated when malignant disease is merely suspected on gastroscopic examination.

We wish to present 3 cases in which the differential diagnosis between hyperplastic gastritis and polyposis or carcinoma was most difficult. In 2 of the cases the roentgen findings suggested carcinoma and were supported gastroscopically in one. In the other it was not available. In both of these, chronic hypertrophic gastritis was the final diagnosis. In the third case, roentgenological studies indicated the presence of a small polyp but at later examination the stomach appeared normal. At gastroscopy the possibility of malignancy was considered, but because of the negative roentgenological findings, a severe hyperplastic gastritis was favored. Subsequently exploratory operation revealed the presence of carcinoma.

**CASE 1.** J. L., a man aged 46 years, was seen in consultation with Drs. Moffitt, Bender and Firestone. Following an accident on May 9, 1935, soreness was present in the right anterior costal margin for months. On July 8, 1935, there was onset of nausea and vomiting after meals at varying intervals, accompanied by a severe cramping pain in the lower abdomen. The vomitus was usually streaked with blood. A loss of 15 pounds occurred in 3 weeks. This condition became progressively worse until August 9, 1935, when he was hospitalized. Under a diet of bed rest and high protein diet, the attacks of vomiting decreased to one per day usually several hours after the evening meal.

Physical examination revealed the presence of marked gastric obesity and evidence suggesting hypo-

cells resembling the lining epithelium of the intestine. Oxyntic cells, especially, had been replaced. The submucosa was scanty and edematous, particularly where it was present in these enlarged folds. The muscularis was not thickened, but contained a few lymphocytes and plasma cells, especially around blood vessels.

**Subsequent course** On October 13, 1939, 13 months after surgery, there were no digestive complaints, and a gain of 7 pounds in weight. A general diet was being followed. Roentgenological examination at this time revealed evidence of a resected stomach, emptying fairly rapidly through a rather large smooth stoma. The remaining portion of the stomach showed evidence of some diffuse hypertrophy of the gastric mucosa, most marked on the lesser curvature just above the stoma.

The history and roentgen findings suggested a polypoid malignancy. At exploration, a definite diagnosis could not be made, although a carcinoma was believed unlikely when the mucosa was exposed through a gastrotomy opening. The question arises whether a patient should be subjected to the serious operation of gastric resection without a positive diagnosis of malignancy. When the possibility of cancer is present, it always dominates the surgeon's mind. With the field exposed and without the assurance of a definite pathological diagnosis, most surgeons would hesitate to close the abdomen without removing the lesion. Frozen section study of gastric wall tissue obtained at biopsy is unsatisfactory for a reliable diagnosis. The tissue is more difficult to study, and there is no certainty that the most characteristic portion of the lesion has been obtained. Moreover, to await thorough study of the tissue obtained at biopsy, would

necessitate a second operation in the event of a positive diagnosis of carcinoma. This procedure would cause unnecessary delay and make for a more difficult later operation, as all surgeons can appreciate. When resection is performed immediately, there is the great satisfaction of knowing that a possible malignancy has been removed. Also, from the experience of ourselves and others (8, 12), such treatment will usually relieve the symptoms of hyperplastic gastritis, which are frequently intractable to medical treatment.

**CASE 2** I C, a woman aged 49 years, was seen March 10, 1939, at the Mount Zion Hospital with Dr. S. Sherman. For 6 months, epigastric distress and postprandial nausea and vomiting had progressively increased, with a weight loss of 10 pounds. Vomiting gave definite relief, alkalies slight relief. Appetite remained fair. Physical examination revealed no abnormalities.

Laboratory examination showed hemoglobin, 75 per cent, red cell count, 4,410,000, white cell count, 6,050. Stools were negative for occult blood. Wassermann and Kahn blood tests were negative. Gastric analysis, using histamine, disclosed free acid 20 after 30 minutes and a total acidity of 40.

Roentgenological and fluoroscopic examination by Dr. J. Levitt, March 14, 1939, revealed evidence of three ulcer craters on the posterior wall in the mid-portion of the stomach, with infiltration in this circumscript area (Fig. 4). There was two-thirds gastric residue at 6 hours. An ulcerated neoplasm was favored.

At gastroscopic examination, March 17, 1939, a funnel-shaped area of ulceration was observed on the posterior wall near the lesser curvature, the ulcer floor appearing hemorrhagic (Fig. 5a). The surrounding mucosa was pale pink in color, moderately nodular and definitely thickened, evidence of an infiltrative process. Superior to the site of ulceration



Fig. 6 Case 2. Section of a mucosal nodulation showing extensive lymphoid follicular hyperplasia, cellular infiltration, and fibrous proliferation.



Fig. 7 Case 3. Drawing of the gastroscopic view of pylorus, antrum and incisura, showing a very irregular, slightly nodular mucosa, thrown into thickened folds.



Fig. 4. Case . Three small dense shadows are present on the posterior wall, in the middle third of the stomach, interpreted as ulcer craters. Fluoroscopically there was evidence of infiltration in this region.

t radiation therapy. In view of the roentgen findings, pre-operative diagnosis was made of carcinoma, probably inoperable.

Operation was performed on September 7, 1938, by the senior author. Palpation disclosed only slight thickening of the gastric wall. There was no induration or enlarged glands, and the liver, pancreas, and gall bladder appeared normal. At the time

gastrostomy revealed the presence of very high, thickened mucosal folds, with intervening deep sulci (Fig. 1). Most of these ridges ran longitudinally, but one fold, about one-half inch wide, ran obliquely posteriorly. There was no evidence of polypoid tumor. In the sulci there were scattered small, round, soft, circumscribed reddish areas, each about 5 millimeters in diameter. The folds were most prominent in the antrum and body and less elevated toward the cardia. No hemorrhagic areas were observed. A large amount of mucus was present. Although the presence of carcinoma was questioned, after deliberation resection was performed. It was felt that such treatment would preclude the possibility of overlooking malignancy. Also, if a periplastic gastritis were present, resection might offer cure of the severe symptoms, which medical therapy had not accomplished. Prolapsed hypertrophic mucosa at the cardia was removed to prevent obstruction of the stomach. Recovery was uneventful.

Pathological examination, performed by Drs. Rusk and Biskind, showed (Fig. 2) the resected specimen showed very marked mucosal hypertrophy with enormously thickened, tortuous elevated, nodular folds. Microscopically (Fig. 3, and b) there was evidence of severe diffuse chronic hypertrophic gastritis. The nodular elevations and hypertrophied folds were composed of mucosa presenting very irregular proliferation, and sharply demarcated by the muscular mucosa. The crypts were elongated, with cork-screw formation and showed striking cystic degeneration. There was dense infiltration of the mucosal stroma by lymphocytes and plasma cells. A increased number of hypertrophied lymphoid follicles were present in the mucosa but absent in the submucosa, and more frequent in the region of the nodular elevations than in the hypertrophied rugal folds. The normal epithelial elements were partially replaced by tall columnar

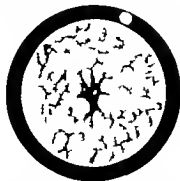


Fig. 5a

Fig. 5. Case . a, Drawing of the gastroscopic lens showing thickened, nodular ulcerated area on the posterior stomach wall, stimulating tumor. b, Drawing of the resected specimen, before fixation, showing localized thickened nodular area on posterior wall, involving lesser curvature and extending to superior edge of specimen. An ulceration is present within this tumor-like area.

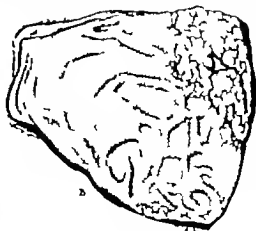


Fig. 5b

cells resembling the lining epithelium of the intestine. Oxyntic cells, especially, had been replaced. The submucosa was scanty and edematous, particularly where it was present in these enlarged folds. The muscularis was not thickened, but contained a few lymphocytes and plasma cells, especially around blood vessels.

Subsequent course. On October 13, 1939, 13 months after surgery, there were no digestive complaints, and a gain of 7 pounds in weight. A general diet was being followed. Roentgenological examination at this time revealed evidence of a resected stomach, emptying fairly rapidly through a rather large smooth stoma. The remaining portion of the stomach showed evidence of some diffuse hypertrophy of the gastric mucosa, most marked on the lesser curvature just above the stoma.

The history and roentgen findings suggested a polypoid malignancy. At exploration, a definite diagnosis could not be made, although a carcinoma was believed unlikely when the mucosa was exposed through a gastrotomy opening. The question arises whether a patient should be subjected to the serious operation of gastric resection without a positive diagnosis of malignancy. When the possibility of cancer is present, it always dominates the surgeon's mind. With the field exposed and without the assurance of a definite pathological diagnosis, most surgeons would hesitate to close the abdomen without removing the lesion. Frozen section study of gastric wall tissue obtained at biopsy is unsatisfactory for a reliable diagnosis. The tissue is more difficult to study, and there is no certainty that the most characteristic portion of the lesion has been obtained. Moreover, to await thorough study of the tissue obtained at biopsy, would

necessitate a second operation in the event of a positive diagnosis of carcinoma. This procedure would cause unnecessary delay and make for a more difficult later operation, as all surgeons can appreciate. When resection is performed immediately, there is the great satisfaction of knowing that a possible malignancy has been removed. Also, from the experience of ourselves and others (8, 12), such treatment will usually relieve the symptoms of hyperplastic gastritis, which are frequently intractable to medical treatment.

CASE 2. I. C., a woman aged 40 years, was seen March 10, 1939, at the Mount Zion Hospital with Dr. S. Sherman. For 6 months, epigastric distress and postprandial nausea and vomiting had progressively increased, with a weight loss of 10 pounds. Vomiting gave definite relief, alkalies slight relief. Appetite remained fair. Physical examination revealed no abnormalities.

Laboratory examination showed hemoglobin, 75 per cent, red cell count, 4,410,000, white cell count, 6,050. Stools were negative for occult blood. Wassermann and Kahn blood tests were negative. Gastric analysis, using histamine, disclosed free acid 20 after 30 minutes and a total acidity of 40.

Roentgenological and fluoroscopic examination by Dr. J. Levitt, March 14, 1939, revealed evidence of three ulcer craters on the posterior wall in the mid portion of the stomach, with infiltration in this circumscript area (Fig. 4). There was two-thirds gastric residue at 6 hours. An ulcerated neoplasm was favored.

At gastroscopic examination, March 17, 1939, a funnel shaped area of ulceration was observed on the posterior wall near the lesser curvature, the ulcer floor appearing hemorrhagic (Fig. 5a). The surrounding mucosa was pale pink in color, moderately nodular and definitely thickened, evidence of an infiltrative process. Superior to the site of ulceration



FIG. 6. Case . Section of a mucosal nodulation showing extensive lymphoid follicular hyperplasia, cellular infiltration and fibrous proliferation.



FIG. 7. Case . Drawing of the gastroscopic view of pylorus, antrum and incisure, showing a very irregular slightly nodular mucosa, thrown into thickened folds.



but thin th nodular circumscribed area mentioned, two small erosions were observed. The roentgenological diagnosis of ulcerated carcinoma was confirmed, although the possibility of a severe hypertrophic gastritis had to be considered in the differential diagnosis.

Operation was performed by the senior thor on March 20, 1930. A localized thickened area was felt the posterior wall of the body near the lesser curvature. Some glands were felt in the lesser and greater omentum. The presence of a carcinoma was questioned by the relative softness of the involved area but could not be definitely excluded. Subtotal gastrectomy was performed, with uneventful recovery.

Pathological examination was made by Drs. Rusk and Blackford. Grossly (Fig 5b) an area of very hypertrophied mucosa, 5 centimeters in diameter was present on the posterior wall near the lesser curvature, extending to the superior edge of the specimen. The mucosa in this region exceeded twice the thickness of the adjacent mucosa, presenting nodular or cobblestone appearance. A small ulceration was present within this infiltrated area, of moderate depth and with induration to the base. No other ulcerations were seen. Microscopically there was marked irregularity of the mucosa of the grossly hypertrophied region, an extended lymphocytic and plasma cell infiltration of the mucosa, and subcutaneous ulceration penetrating through the muscularis in some. There were multiple minute cut ulcerations. An increased number of hyperplastic lymphoid follicles penetrated and distended the muscularis mucosae (Fig 6). The glands did not show the loss of the differentiated cellular constituents. The crypts were deep and slightly tortuous. The submucosa was moderately thickened as result of edema, fibrous proliferation and pronounced cellular infiltration. Two lymph nodes obtained from the lesser and greater omentum were hyperplastic. The pathological diagnosis was that of localized chronic ulcerative hypertrophic gastritis.

Subsequent course. On January 5, 1930, months after operation, the patient was symptom free. Roentgenological examination on May 2, 1930, revealed no abnormalities other than evidence of previously resected stomach.

In this case as in the first, carcinoma was suspected roentgenologically. But in addition the diagnosis was confirmed gastroscopically because of the thickened nodular ulcerated area observed. As in Case 1 chronic hypertrophic gastritis was the final pathological diagnosis. At operation, however there was more evidence to support the possibility of carcinoma than in the preceding case. It is interesting to note that the lesion here was more limited in extent than in Case 1. A rather similar case of localized hypertrophic

gastritis, mistaken for an infiltrating type of neoplasm gastroscopically, was reported from the Massachusetts General Hospital (13). The roentgenologists there differed in opinion, one interpreting the localized character of the lesion as an argument against the presence of gastritis and in favor of neoplasm.

CASE 3. S. P. man aged 6 years, born July 1, 1930, with Dr. S. Burr, Eureka, and Dr. J. Smith. The patient complained of epigastric distress after meals for months accompanied by slight distention. A bland diet and trophic afforded partial relief. There was no weight loss.

Physical examination disclosed thin, obese male of healthy appearance, with slight epigastric tenderness.

Laboratory examination showed hemoglobin, 81 per cent red cells, 4,500,000 hit cells, 6,650. Stools contained no occult blood. Wassermann and Kahn blood tests were negative. Gastric analysis using histamine, showed absence of free hydrochloric acid in 3 specimens and total acidity of 0.

Roe gastropological examination elsewhere, month before entry revealed evidence of small round filling defect, centimeter in diameter at the junction of the middle and lower thirds of the stomach near the lesser curvature, interpreted as single polyp. Another examination as performed July 1, 1930, and the suprapubic area as believed to be produced by redundant mucosa and not by true polyp. The mucosa appeared uninterrupted, and peristalsis was normal through this region.

Gastroscopic examination was performed on July 3, 1930, with the following findings. The mucosal aspect of thetrum and incisura was distorted owing to the presence of very irregular slightly nodular mucosa throughout thickened folds (Fig 7). On the posterior wall near the lesser curvature, above the incisura, very hypertrophied and hyperemic fold projected well prominently toward the lumen of the stomach. On the lesser curvature, on anterior wall of the body the mucosa was thickened, irregular and slightly nodular with two small benign orthopic areas observed. A diagnosis made of severe chronic hypertrophic gastritis of the distal half two-thirds of the stomach, most marked on the posterior wall at the junction of the middle and distal thirds near the lesser curvature. A true polyp as observed. In the differential diagnosis, the presence of diffusely infiltrating neoplasm had to be strongly considered. However since the clinical history and roentgenological findings are compatible with benign lesion, the presence of severe chronic gastritis was favored, and observation advised.

Subsequent course (communication from Dr. Burr, Eureka). Epigastric distress flatulence, and belching progressively increased. A mass developed in the right upper quadrant of the abdomen, near the gall-bladder region. Roentgenological studies, \

vember 8, 1939, revealed evidence of infiltration of the stomach wall, involving the distal third and extending along the lesser curvature posteriorly to the junction of the upper and middle third. Operation, November 13, 1939, revealed the presence "of an advanced carcinoma of the stomach, occupying the entire posterior wall, over an inch thick throughout and inoperable." A large metastatic lesion was observed in the liver. A biopsy revealed the presence of a scirrhous type of carcinoma. On November 17, 1939, the patient expired. Consent for autopsy was not obtainable.

This case presents the converse of the 2 other cases described, and shows that carcinoma may simulate gastritis, as has been observed by others (1, 2, 3, 14, 18). The first roentgenological examination suggested the presence of a single gastric polyp. Repeated examination elsewhere within 1 month demonstrated no definite lesion. It is interesting that gastroscopy at this time disclosed evidence of diffuse infiltrative changes, especially on the posterior wall. However, a severe hypertrophic gastritis was incorrectly favored, although a diffusely infiltrating carcinoma was considered in the differential diagnosis. Four months later, pronounced changes could be observed in roentgenological studies. The case re-emphasizes the fact that in certain instances gastroscopy, as well as x-ray examination, may fail in the differentiation of the two lesions.

#### SUMMARY AND CONCLUSIONS

Three cases are presented, in two of which a pre-operative diagnosis of gastric carcinoma was made when marked chronic hypertrophic gastritis was the pathological diagnosis. In the third case, a severe hypertrophic gastritis was favored, but carcinoma was discovered at subsequent operation. A fourth case, the first description in the literature of hypertrophic gastritis simulating tumor, is briefly discussed again 14 years later.

Chronic hyperplastic gastritis simulating carcinoma is probably more prevalent than has been suspected. The increasing number of cases reported recently supports this belief. Gastroscopy has stimulated more interest in this subject.

The differential diagnosis between severe hyperplastic gastritis and carcinoma may oc-

asionally be difficult or impossible, not only by roentgen and gastroscopic examination, but also at surgical exploration. It should be emphasized that unusual cases such as these in no way detract from the value of gastroscopy as a diagnostic aid.

A knowledge of this subject is of importance to the surgeon. When the diagnosis is doubtful, exploratory operation is definitely indicated. If this procedure does not furnish the answer, resection appears advisable to avoid the danger of overlooking a malignancy, as well as to establish the final diagnosis.

#### BIBLIOGRAPHY

1. BENEDICT, E. M. Chronic gastritis, clinical discussion based on gastroscopic examination. *New England J Med*, 1935, 212 468-472.
2. Idem. Gastroscopic observations in neoplasm. *New England J Med*, 1936, 214 563-566.
3. Idem. Importance of gastroscopy in surgical diagnosis. *Am J Surg*, 1938, 40 5-11.
4. BRUNN, H., and PEARL, F. Diffuse gastric polyposis, adenopapillomatosis gastrica. *Surg, Gynec & Obst* 1926, 43 559-598.
5. CROHN, B. B. Chronic gastritis, clinical aspects. *Bull New York Acad Med*, 1939, 15 392-405.
6. EUSTERMANN, G. B. Gastritis problem. *South M J*, 1936, 29 684-693.
7. FABER, K. Gastritis and Its Consequences. Pp 44, 112. New York: Oxford University Press, 1935.
8. LOFFCKEN, H. Beiträge zur Klinik und Operation der tumorähnlichen hypertrophischen Gastritis. *Beitr z klin Chir* 1938, 168 177-183.
9. KANTOR, J. L. Giant rugae (localized hypertrophic gastritis) resembling carcinoma. *Am J Roentgenol*, 1936 35 204-207.
10. KONJETZNY, G. E. Chronische Gastritis und Magenkrebs. *Monatschr f Krebs*, 1934, 2 65-78.
11. Idem. Ueber die Anzeige zur chirurgischen Behandlung der Gastritis zur Beurteilung ihrer Ergebnisse. *Therap d Gegenw*, 1934, 75 65-70.
12. Idem. Eine besondere Form der chronischen hypertrophischen Gastritis unter dem klinischen und roentgenologischen Bilde des Carcinoms. *Chirurg*, 1938 10 260-268.
13. LINGLEY, J. R. Case report from the weekly seminar of the Department of Roentgenology, Massachusetts General Hospital. *Am J Roentgenol*, 1939, 42 438-441.
14. MOUTIER, F. *Traité de gastroscopie et de pathologie endoscopique de l'estomac*. Paris: Masson et Cie, 1935.
15. SCHINDLER, R. Gastroscopy. *The Endoscopic Study of Gastric Pathology*. P 207. Chicago: University of Chicago Press, 1937.
16. Idem. Gastritis simulating tumor formation. *Am J Digest Dis*, 1939, 6 523-520.
17. Idem. Personal communication to the authors.
18. SCHINDLER, R., and GOLD, R. L. Gastroscopy in gastric carcinoma, especially in its early diagnosis. *Surg, Gynec. & Obst.*, 1939, 69 1-17.

# THE EFFECT OF REPEATED PREGNANCIES ON RABBITS WITH RENAL HYPERTENSION

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THE hypertensive syndromes which occur during pregnancy have been a great source of annoyance to those clinicians and obstetricians who have tried to classify them with regard to symptomatology and to prognosis, both immediate and remote for mother and fetus. In the human the co-existence of pregnancy with hypertension or renal disease is believed to be harmful to the kidney and vascular system of the mother and to carry an extremely poor prognosis for the fetus.

The production of chronic renal disease in the experimental animal has been very difficult and uncertain by most of the methods usually used to produce renal injury. Uranium nitrate, mercuric chloride, bacterial toxins, and nephrotoxic serum all produce substantial renal lesions of an acute nature but the chronic picture is difficult to attain, uncertain in quality, and but few of the animals live to attain a true chronic status. Hypertension is usually absent in animals in which renal injury is produced by these methods although x-ray and resection of a large amount of the functioning renal tissue do produce significant elevations of the blood pressure.

The recent development of a method which produces a marked elevation of the blood pressure with minimal amounts of demonstrable renal injury has paved the way for studying many of the phases of hypertension. The application of this procedure to the pregnant animal has been shown to produce a syndrome which resembles eclampsia in many features.

The syndrome produced by renal ischemia in the pregnant animal is strikingly similar to eclampsia in the human, and the course followed by these animals during subsequent

pregnancies is not unlike that of patients with pregnancy complicated by hypertensive disease or chronic nephritis.

These factors have led us to attempt to determine what effect repeated pregnancies may have on groups of animals in which hypertension had existed for some time and to find out some of the factors which may have a bearing on the course of the disease as well as on the prognosis for the fetus.

## MATERIALS AND METHODS

Twelve non pregnant rabbits of 2.5 to 3 kilograms body weight and of varying breeds and ages were used as experimental animals. All were purchased from a local dealer and were healthy and disease free as far as could be determined by the general condition and by the appearance of the viscera at laparotomy.

A control period of 3 weeks was carried out in which blood pressures were taken twice weekly by an indirect method, urine<sup>2</sup> examinations for sediment, albumin and specific gravity, and blood chemistry<sup>3</sup> studies were done weekly. In addition the animal was weighed, the eye-grounds examined by the ophthalmoscope and the general condition noted.

Following this control period the abdomen was opened under sterile technique and the aorta was constricted to degrees varying from

Following the local application of styli to the ear of the rabbit, summer dilatation of these vessels, the splanchnic pulse as palpated. After the constriction of the aorta has been put into effect, small coils of cotton gauze or small cuff, applied around the base of the ear. Indirect blood pressure readings can then be made by palpation. These readings have checked with mercury manometer readings of the carotid artery in rabbits with constricted blood pressures. In severe sections of less than 20 millimeters mercury.

From the tested qualitatively by albumin by the best and acetic acid test, the specific gravity was determined by a hydrometer, and careful microscopic examinations were shown on sediment obtained by centrifuging at low speed.

These studies consisted of measurements of non protein nitrogen, urea acid, and urea. In few animals, however, determinations were done by the method of Landolt.

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$\frac{1}{4}$  to  $\frac{3}{8}$  of the original cross-sectional area by a silver wire loop both proximal and distal to the points of origin of the renal arteries

For a period of 15 days after the constriction of the aorta had been carried out, the blood pressure determinations were done daily, urine examinations and determination of blood chemistry were carried out every other day, and the animals were weighed weekly. Following this initial period blood pressure determinations were done twice weekly, urine was examined weekly, and weighing was carried out at semi-monthly intervals. Blood chemistry determinations and inspection of the eye-grounds were carried out at monthly intervals.

All animals were kept on this regimen for periods varying from 1 to 9 months before being allowed to become pregnant for the first time.

After the first pregnancy had terminated, a control period of 1 month was observed before the next pregnancy occurred. When conception did not occur at the scheduled time, the animal was again exposed to the male at 15-day intervals until pregnancy or death occurred.

Fetuses were recorded as to length, condition, and number, and then discarded.

Following exposure to the male the abdomen was gently palpated twice weekly. Fetuses could usually be palpated after 12 days of gestation, and resorption could be determined after this time by failure of the fetal ovoids to grow or by their sudden decrease in size or absence.

Six animals were allowed to live their full life term and the 6 remaining were sacrificed by the intravenous injection of 2 cubic centimeters of 40 per cent formalin. Following death, a complete autopsy was done within 4 hours and sections of all viscera, glands of internal secretion, and, on some occasions, bone marrow were taken.

#### CONTROLS

Nine non-pregnant female rabbits with aortic constriction proximal to the points of origin of the renal arteries were included in control group 1. A preliminary control period similar to that described for the experimental animals



Fig 1 Kidneys showing depressions of the cortex. No adherence of the capsule was noted here despite the marked "scarring."

was observed in this group. Following aortic constrictions of varying degrees, these animals were observed for varying lengths of time. 2 animals were observed for 9 months, 2 for 6 months, 2 for 4 months, and 2 for 3 months. Four of these animals died, and the 4 remaining, still in good health, were then used as experimental animals in the pregnancy series. One animal, followed for a year, was sacrificed.

Three female rabbits with aortic constriction carried out to reduce the lumen to  $\frac{1}{4}$  of the original cross-sectional area distal to the points of origin of the renal arteries composed control group 2. Following a preliminary period of observation, 3 months for animal 1, 4 months for animal 2, and 6 months for animal 3, each of these animals was subjected to repeated pregnancies.

Clinical observations, blood pressure determinations, urine examinations, and blood chemistry estimations were studied in both control groups according to the schedule given for the experimental group and complete autopsies were done.

#### RESULTS

We are unable to make a definite statement regarding the effect on longevity of repeated



Fig. 2.

Fig. 2. Renal cortex showing an area of scarring, atrophy of tubular tissue, thickening of arterioles, and of Bowman capsule. Note condensation of glomeruli. (Hematoxylin and eosin.)



Fig. 3.

Fig. 3. Renal cortex showing tubular atrophy but no evidence of interstitial reaction. (Hematoxylin and eosin.)



Fig. 4.

Fig. 4. Glomerulus showing hyalineization of one of the capillary tufts. (Hematoxylin and eosin.)

pregnancies in animals with renal hypertension because of the small series, the number sacrificed and the presence of intercurrent pulmonary infection in several of the animals. We have gained the general impression that repeated pregnancy does have a detrimental effect on longevity. During the period of gestation no significant change in condition of the animals was noted, and when depression was noted it was usually seen immediately following delivery. Only one animal died while pregnant and but one immediately following delivery; the remainder died in the interval between pregnancies and the pathological findings in these animals were not unlike those of the remaining hypertensive pregnant animals.

Five of the animals conceived once and never again became pregnant. Three animals conceived twice; 3 had 3 litters and 1 became pregnant 4 times.

Of the first pregnancies 58 per cent ended in resorption, 12 per cent in premature deadborn fetuses, and 30 per cent in term deliveries. Of the second pregnancies 28 per cent ended in resorption, 28 per cent in premature deliveries, and 44 per cent delivered living term fetuses. Fifty per cent of the third pregnancies were resorbed and the remainder went to term.

The animal pregnant for the fourth time delivered normal living term fetuses. It seems that the multigravid animal has a slightly better chance of obtaining living term fetuses.

The degree of aortic constriction played a definite part in the outcome of the pregnancy. Of the animals with 4 plus constriction, 50 per cent of the pregnancies resulted in delivery of premature deadborn fetuses and 38 per cent in resorption of fetuses, while of those animals with 2 plus constriction 46 per cent delivered term fetuses, 6 per cent premature deadborn fetuses, and 48 per cent resorbed the fetuses.

Little effect was noted in relation to the length of time hypertension had been present before pregnancy had occurred. In animals becoming pregnant 1 month following aortic constriction 25 per cent of the fetuses went to term while the remainder were resorbed. Of those in which 4 months had elapsed before pregnancy there resulted 50 per cent term fetuses, 25 per cent premature, and 25 per cent resorbed. In animals in which 6 months had elapsed between constriction and pregnancy, 25 per cent went to term and 75 per cent resorbed; of those in which 9 months had elapsed 50 per cent went to term and 50 per cent resorbed.

An increase in blood pressure was noticeable in all animals at the end of 1 month. Four animals averaged less than 20 millimeters mercury systolic pressure increase over the control level, 6 averaged 20 to 40 millimeters mercury systolic pressure increase, and 2 constantly maintained above 50 millimeters mercury increase in systolic pressure. All animals with 4 plus constriction maintained a pressure of above 150 millimeters mercury, 3 of the animals with 2 plus constriction maintained this level or better, while the one animal with 1 plus constriction rarely attained more than 140 millimeters mercury.

No definite effect of the presence of a pregnancy on the blood pressure findings was noted. It has been a noticeable but not constant finding that the blood pressure seems to be more unstable during the pregnancy, particularly the first one. As long as the animal remains in good condition, the blood pressure remains elevated and in a few animals there tends to be a gradual minimal increase in level.

Urine findings are for the most part negative during the earlier stages of the process. Albuminuria is noted at inconstant intervals in minimal amounts in the early stages of the hypertension and more frequently and in slightly greater amounts toward the end of the course, although usually no more than a heavy trace is seen. An increase in renal injury, as evidenced by more severe albuminuria or increased numbers of casts in the urine, was not noted during pregnancy.

Blood pressure and urine findings in representative experimental animals are presented in Charts 1, 2, 3, and 4<sup>1</sup>.

The blood chemistry findings in both the pregnant and the non-gravid state showed no significant variation from the control values.

Weight and clinical condition usually ran parallel. With approach to term a gain in weight of 200 to 300 grams was noted, most of which was lost immediately following delivery.

Examination of the eye-grounds failed to show recognizable thickening of the vessels. Occasionally definite spasm was made out,

although the labile condition of the rabbit's arterial tree makes subjective evaluation of spasm almost impossible. A moderate amount of tortuosity was noted to develop in 3 animals. No hemorrhages or exudates were seen.

#### PATHOLOGY

In general the animals showed some evidence of recent weight loss, and 2 animals were obviously chronically debilitated. In 2 animals small chronic stitch abscesses were noted, but in all no evidence of a generalized peritoneal or pleural inflammatory process was noted.

*Heart* The heart showed marked left ventricular hypertrophy in 3 of the animals, moderate in 5, and no noticeable change in 4. Grossly, these organs showed no evidence of hemorrhage, scarring, or marked fatty change. The papillary muscles and chordæ tendineæ showed hypertrophy when the left ventricular muscle was definitely thickened. Microscopically, these myocardia usually showed no evidence of scars although in a few areas one gets the impression that there is a minimal amount of diffuse fibrous tissue proliferation and occasionally one finds small collections of round cells and fibroblasts.

*Lungs* Two animals showed definite consolidation of the lung in which the *Bacillus bronchisepticus* could be isolated. In 6 of the remaining animals in which death occurred spontaneously, 4 had definite pulmonary edema, and in the 2 others no definite gross lesions could be made out.

*Adrenal* The adrenals grossly were hypertrophied in 8 cases. This hypertrophy was confined almost entirely to the cortex and occurred bilaterally and equally. No adenoma formation was noted. The adrenal hypertrophy noted grossly was thought to be cortical for the main part and staining by scharlach R showed all layers of the cortex save the zona glomerulosa heavily packed with fat.

In 10 animals, cells or collections of cells were found containing fatty material and cholesterol clefts. These cells occasionally attained such proportions as to occupy  $\frac{1}{10}$  to  $\frac{1}{6}$  of the entire cross section of the gland. Areas of necrosis were present in 2 of these larger cell nests.

<sup>1</sup>In the charts and in the descriptive material, 4 plus or severe constriction indicates reduction of the cross sectional diameter of the aorta to  $\frac{1}{4}$ ; 2-plus or moderate constriction, reduction to  $\frac{1}{2}$ ; and 1 plus or mild constriction, reduction to  $\frac{3}{4}$  of the original cross-sectional diameter.

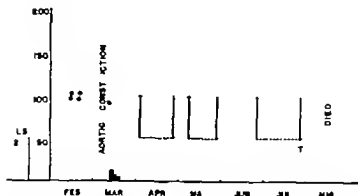


Chart 1. Blood pressure and urine changes accompanying three pregnancies in an animal with moderate constriction of the aorta proximal and distal to the points of origin of the renal vessels. The first pregnancy in this animal occurred 1 month following aortic constriction. (Rabbit No. 80.)

Note. In this and the following charts albuminuria is expressed as: Traces, Clouding after acid but not after heating; + light granular precipitation after heating; + moderate granular precipitation after heating; ++ heavy flocculate precipitation after heating. † indicates conception; ‡ indicates the end of the period of gestation; R, indicates resorption of fetuses; P indicates premature delivery; T indicates term fetuses delivered.

**Liver.** Grossly the liver in these animals showed little deviation from normal. The size of the liver depended greatly on the state of nutrition of the animal. Spontaneous liver disease coccidiosis, cholangitis, etc. were observed to a minimal degree in 2 animals. No cirrhosis of any type was noted and microscopic changes of significance in these animals were not encountered.

**Kidneys.** The kidneys of 3 of these animals showed no gross lesions while in the 9 remaining there were definite multiple depressions occurring in both kidney cortices varying in size from 0.5 to 1.0 millimeter in diameter to 1.0 to 1.5 centimeters in diameter. They were dark, retracted and resembled scarring of the

kidney cortex with retraction (Fig. 1). It is of interest, however, that the capsules of the kidneys were usually not adherent to such areas of injury. The medullary portions and the pelvis were not remarkable. No evidence of ureteral or pelvic dilatation or inflammation was noted.

Microscopic study of these kidneys showed areas which were characterized by condensation of the malpighian corpuscles with concentration of the nuclei in the glomeruli. Bowman's capsule was usually thickened and the tubules in these areas were seen only in remnants. The lining cells of these tubules were usually flattened and contained small dark nuclei. The lumina were dilated and

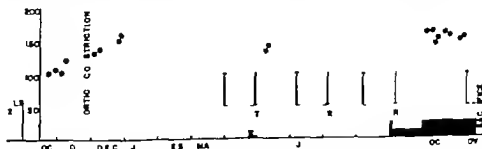


Chart 2. Blood pressure and urine changes in an animal following severe constriction of the aorta proximal and distal to the points of origin of the renal arteries during four pregnancies. The first pregnancy occurred 4 months following aortic constriction. (Rabbit No. 8.)

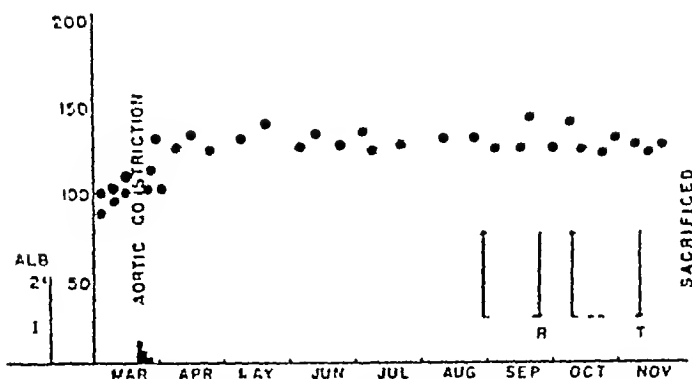


Chart 3. Blood pressure and urine findings during two pregnancies in an animal in which the aorta had been moderately constricted. The first pregnancy occurred 6 months following the development of hypertension (Rabbit No. 21)

usually contained hyaline casts. The interstitial tissue consisted of dense scar tissue with varying amounts of round cell infiltration. Arteriolar thickening was marked in such areas (Fig. 2).

In 6 animals definite areas of atrophy of the tubular epithelium were noted (Fig. 3). In 3 animals definite hyaline thrombi in several of the glomeruli were noted (Fig. 4). This was not a striking finding, however. Basement membrane thickening was carefully looked for and more than an occasional thickening of one tuft could not be demonstrated. Definite round cell infiltration of the pelvis and pyramids could be shown in only one animal.

*Ovaries and uterus.* No specific changes could be made out in these organs.

*Aorta.* Grossly, all but 3 of the 8 aorta examined showed evidence of atheromatous plaque formation in the thoracic and upper abdominal aorta. These plaques varied in size from pin-point yellow flakes to flat yellowish, white shiny areas 3 to 5 millimeters in

length 1 millimeter in width, and were noticeably elevated. These were most noticeable in the arch and the upper thoracic portion of the aorta and frequently, although not exclusively, around the mouths of vessels.

Microscopically, the yellowish plaques described grossly showed that the intima was thickened by the infiltration of pale-staining, amorphous material with diffusely scattered nuclei of wandering cells. Fat stains on these plaques showed that the amorphous material contained a large amount of material which stained with scharlach R, most of which seemed to be contained in the macrophages. Elastic tissue stains showed definite reduplication and fibrillation of the internal elastic lamella in many of these areas.

*Gut.* No evidence of ulceration, hemorrhage, or membrane formation was noted and, microscopically, the mucosal and the muscular layers were normal.

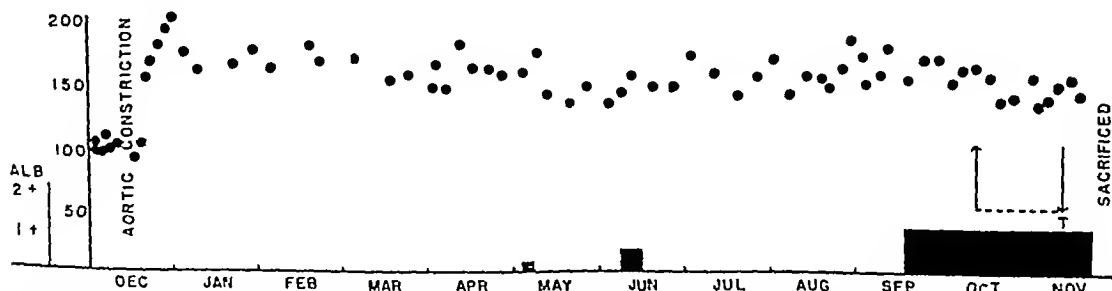


Chart 4. Blood pressure and urine findings in an animal with severe aortic constriction proximal and distal to the points of origin of the renal arteries followed by pregnancy 9 months after development of hypertension (Rabbit No. 17)



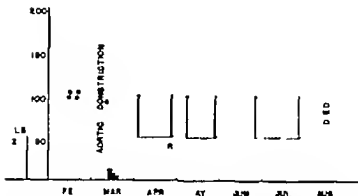


Chart 2. Blood pressure and urine changes accompanying three pregnancies in an animal with moderate constriction of the aorta proximal and distal to the points of origin of the renal vessels. The first pregnancy in this animal occurred 4 months following aortic constriction. (Rabbit No. 80.)

Note: In this and the following charts albuminuria is expressed as: Trace, Clouding after acid but not after heating, + light granular precipitation after heating, ++ moderate granular precipitation after heating, +++ heavy flocculate precipitation after heating. † indicates conception, ‡ indicates the end of the period of gestation, R, indicates resorption of fetuses; F indicates premature delivery; T indicates term fetuses delivered.

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kidney cortex with retraction (Fig. 1). It is of interest however that the capsules of the kidneys were usually not adherent to such areas of injury. The medullary portions and the pelvis were not remarkable. No evidence of ureteral or pelvic dilatation or inflammation was noted.

Microscopic study of these kidneys showed areas which were characterized by condensation of the malpighian corpuscles with concentration of the nuclei in the glomeruli. Bowman's capsule was usually thickened and the tubules in these areas were seen only in remnants. The lining cells of these tubules were usually flattened and contained small dark nuclei. The lumina were dilated and



Chart. Blood pressure and urine changes in an animal following severe constriction of the aorta proximal and distal to the points of origin of the renal arteries during four pregnancies. The first pregnancy occurred 4 months following aortic constriction. (Rabbit No. 8.)

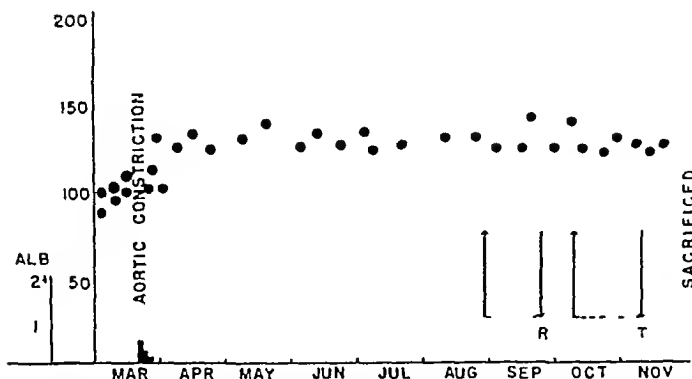


Chart 3 Blood pressure and urine findings during two pregnancies in an animal in which the aorta had been moderately constricted. The first pregnancy occurred 6 months following the development of hypertension (Rabbit No. 21)

usually contained hyaline casts. The interstitial tissue consisted of dense scar tissue with varying amounts of round cell infiltration. Arteriolar thickening was marked in such areas (Fig. 2).

In 6 animals definite areas of atrophy of the tubular epithelium were noted (Fig. 3). In 3 animals definite hyaline thrombi in several of the glomeruli were noted (Fig. 4). This was not a striking finding, however. Basement membrane thickening was carefully looked for and more than an occasional thickening of one tuft could not be demonstrated. Definite round cell infiltration of the pelvis and pyramids could be shown in only one animal.

*Ovaries and uterus* No specific changes could be made out in these organs.

*Aorta* Grossly, all but 3 of the 8 aorta examined showed evidence of atheromatous plaque formation in the thoracic and upper abdominal aorta. These plaques varied in size from pin-point yellow flakes to flat yel-

lowish, white shiny areas 3 to 5 millimeters in length, 1 millimeter in width, and were noticeably elevated. These were most noticeable in the arch and the upper thoracic portion of the aorta and frequently, although not exclusively, around the mouths of vessels.

Microscopically, the yellowish plaques described grossly showed that the intima was thickened by the infiltration of pale-staining, amorphous material with diffusely scattered nuclei of wandering cells. Fat stains on these plaques showed that the amorphous material contained a large amount of material which stained with scharlach R, most of which seemed to be contained in the macrophages. Elastic tissue stains showed definite reduplication and fibrillation of the internal elastic lamella in many of these areas.

*Gut* No evidence of ulceration, hemorrhage, or membrane formation was noted and, microscopically, the mucosal and the muscular layers were normal.

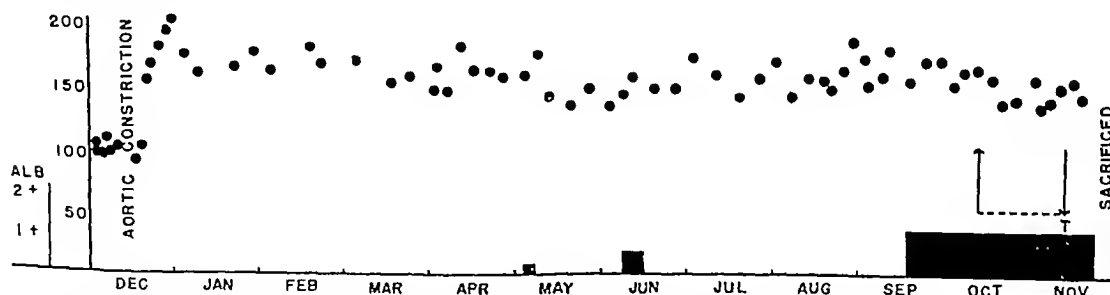


Chart 4. Blood pressure and urine findings in an animal with severe aortic constriction proximal and distal to the points of origin of the renal arteries followed by pregnancy 9 months after development of hypertension (Rabbit No. 17)

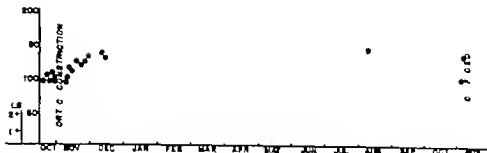


Chart 5. Blood pressure and urine findings in an animal with minimal aortic constriction proximal and distal to the points of origin of the renal vessels. (Rabbit No. 5)

**Parathyroids** In 3 animals a definite enlargement of the parathyroid tissue could be made out. This was not certain in the remaining animals in the gross although 3 additional animals showed striking amounts of parathyroid tissue in sections of the thyroid gland.

No pathology could be found in the brain, pituitary thyroid or bone marrow.

#### CONTROLS

**Control group 1** In this group were 9 animals with aortic constriction proximal and distal to the points of origin of the renal vessels and in which no pregnancy had occurred. The length of life in this group is not significant as it contained animals which died or were sacrificed early in the experiment. None of these animals was given an opportunity to become pregnant. All animals showed an increase in blood pressure. Two attained pressures which averaged more than 50 millimeters mercury above the control level and 2 averaged from 20 to 40 millimeters mercury above, while the 5 remaining maintained average pressures of less than 20 millimeters mercury above the control level. The general curves of blood pressure levels were identical with those of the experimental group.

Urine findings were usually negative only 2 animals had mild albuminuria and cylindruria immediately following aortic constriction. Chart 5 shows the effect of this procedure on a representative animal. Minimum pressure elevation and no urinary changes were noted. Blood chemistry findings showed no significant variation from normal. Weight changes were not remarkable and the eye grounds showed no significant changes.

All pathological changes noted in the experimental group were present in the 5 animals of this group which were examined but to a much less marked degree. This is easily correlated with the length of time these animals were hypertensive and with the degree of elevation in pressure sustained.

**Control group 2** In this group were 3 animals in which aortic constriction had been performed distal to the points of origin of the renal vessels. The clinical condition and weight remained good and fairly constant throughout the experiment. All these animals were sacrificed. In none was a significant persistent elevation of blood pressure noted although one animal showed a low grade elevation of pressure beginning 20 days following aortic constriction and lasting approximately 1 month. The urine remained constantly negative for albumin cells, and casts. Blood pressure and urine findings during the experiment are demonstrated for a representative animal in Chart 6. Weight changes were noted only during pregnancy and were similar to those noted in the experimental group. Eye-grounds showed no significant variation from normal. No deviation from normal was produced in these functions by pregnancy. The positive findings at postmortem were limited to a minimal spontaneous nephritis. The aortas were searched for atheromatous plaques and none found.

#### ANALYSIS OF STUDY

We are at a loss to explain why reducing the renal blood flow in the pregnant animal produces a fatal vasospastic syndrome while pregnancy in the animal with reduced renal blood flow produces little, if any effect.

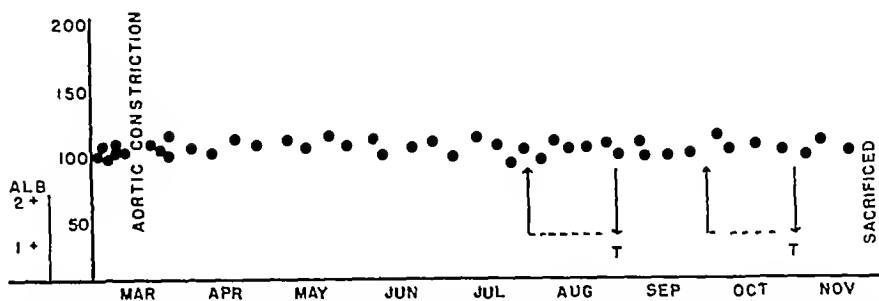


Chart 6 Blood pressure and urine findings on an animal with constriction of the aorta distal to the points of origin of the renal vessels. Two pregnancies were experienced during this period, both of which went to term (Rabbit No. 37)

It seems probable that the life expectancy of hypertensive animals is decreased by repeated pregnancies. The cause of death is usually a secondary infection which has superimposed itself upon general debility. It seems likely that cardiac failure, vascular accident, and renal failure would account for a fair proportion of the deaths, as is seen in the human with hypertensive diseases and eclampsia, had not early death taken place by secondary causes.

Fetal prognosis is quite poor in these animals, only 40 per cent of the pregnancies resulting in living term fetuses. This is quite similar to the condition existing in the human with chronic nephritis in which a similar high fetal mortality rate is noted. The mechanism for this low proportion of living fetuses, both in the rabbit with hypertension and in the human nephritic that suggests itself is anemia to the uterus by the severe vasospasm which leads to placental anemia and infarction and fetal death with expulsion or resorption.

The length of time elapsing between the production of hypertension and the first pregnancy, and the degree of hypertension seemed to play no part in prognosis for the fetus, although there seems to be a definite increase in number of term fetuses with succeeding pregnancies and with minimal degrees of aortic constriction.

It is noticeable that the degree of aortic constriction is usually parallel to the degree of hypertension, the incidence of albuminuria, the degree of renal damage, cardiac hypertrophy, and the degree of atheromatous plaque formation in the aorta. All of these factors were also accentuated by time when more

than a minimal amount of hypertension existed.

We have been unable to demonstrate that repeated pregnancies alter the course of these hypertensive animals. No evident change in the blood pressure levels can be demonstrated, and urine findings show no significant changes when compared with control animals with the same degree of injury. An attempt was made to do renal function tests, but these were considered of no value due to the remarkable variations in clearance values obtained in control animals. This failure to find a rise in tension and increase in albuminuria seems to be in direct contrast to what is found on the human with chronic nephritis in which the classical course is a rise in blood pressure during the early parts of pregnancy to a fall during delivery, but to a level a little higher than that noted before the pregnancy.

The pathological findings, particularly of the kidney, aorta, and adrenals, are noteworthy.

The failure to demonstrate arteriolar changes in the eye-grounds of these animals is disappointing but perhaps not strange, as the labile vascular system of this animal makes objective determinations of this nature difficult in minimal grades of arteriolar thickening. The changes in the arteriolar tree in other portions of the animal, however, bear comment, as moderate amounts of thickening are quite definite in the brain and kidney.

We believe that these studies have definite bearing on the attempt to link the toxemias of pregnancy and their sequelae to the nephroscleroses by a common etiological agent.

The most recent and probably the most satisfactory classification of the toxemias of pregnancy has been based on the degree of hypertension, albuminuria, and vascular and renal damage as evidenced during and following pregnancy. In the follow-up of such patients one is impressed with the evidence that, although many have further pregnancies with no evidence of hypertension or vascular and renal pathology in others the disease has not ceased with the delivery of the baby since as many as 50 per cent develop what is later classified as essential hypertension chronic nephritis, or one of the subdivisions of this group of syndromes. We are also cognizant of a small group of these patients who have mild toxemia of pregnancy with the first baby essential hypertension with the following, and chronic nephritis with the third. There seems to be little doubt that in most patients repeated pregnancy tends to accentuate this rate of progression.

It seems likely that the severity of the toxemia parallels the degree of reduction of renal blood flow which occurs during gestation and that the subsequent course is determined by the renal and vascular status prior to pregnancy in addition to the permanent vascular damage produced by the prolonged vascular spasm associated with that type of gestation.

#### CONCLUSIONS

Repeated pregnancies in rabbits with varying degrees of hypertension produced by renal ischemia have no noticeable effect on blood pressure, albuminuria, or histological renal changes.

The life expectancy of these animals seems to be decreased.

Fetal resorption and death occurs in a large percentage of these animals.

Adrenal, renal, and aortic histological changes are reported.

The evidence for a common etiological agent of the 'toxemias of pregnancy' and the nephrosclerotic is supported.

#### BIBLIOGRAPHY

BELL, E. T. and CLAWSON, B. J. Primary (essential) hypertension, study of four hundred and twenty cases. *Arch. Path.*, 1928, 9, 937.

2. CHRISTIAN, H. Discussion of article by J. E. Priden, Ultimate results of essential hypertension. *J. Am. M. Ass.*, 1926, 87, 925.
3. DE LEE, J. B. Principles and Practice of Obstetrics. Chap. 7. Philadelphia: W. B. Saunders Co., 1931.
4. DELL, L. and EISENBERG, C. C. Eclampsia-like syndrome occurring in pregnant dogs and rabbits following renal artery constriction. *Proc. Soc. Exper. Biol. & Med.*, 1934, 37, 261.
5. Idem. The effect of renal artery constriction in the pregnant rabbit and other endocrine states. (In press.)
6. DELL, L. V. IEDERHOFF, C. E., and CARSON, J. F. The effect of quantitative reduction of renal blood flow upon the pregnant rabbit. *J. Clin. Invest.*, 1934, 3, 64.
7. DUVAL, C. W. and HUBBARD, R. J. Experimental glomerulonephritis induced in rabbits with the endotoxic principle of streptococcus scarlatinae. *J. Exper. Med.*, 1928, 44, 367.
8. FOLIN, O. Improved method for determination of uric acid in blood. *J. Biol. Chem.*, 1926, 86, 179.
9. FOLIN, O. and WU, H. A system of blood analysis. *J. Biol. Chem.*, 1924, 8, 15.
10. GOLDBLATT, H., LYONS, J., HANNA, R. F. and SCHNEFFEL, W. W. Studies on experimental hypertension. I. The production of persistent elevation of systolic blood pressure by means of renal ischemia. *J. Exper. Med.*, 1934, 59, 347.
11. HARTMAN, F. W., BOLLINGER, A., and DOWD, H. P. Experimental nephritis produced by irradiation. *Am. J. M. Sc.*, 1928, 17, 487.
12. HODGES, W. C. Experimental study of acquired resistance of the rabbit's renal epithelium to urinary albumin. *Ann. Int. Med.*, 1934, 7, 747.
13. Idem. Regeneration of tubular epithelium in the ischemic kidney following injury by mercuric chloride. *Ann. Int. Med.*, 1935, 4, 65.
14. LEVINSKY, F. C. A Textbook of Obstetrics for Students and Practitioners, Chap. 1. New York: Macmillan Co., 1928.
15. KAPLAN, B. I. and SMITH, H. W. Excretion of leucine, creatinine, xylitol and urea in the normal rabbit. *Am. J. Physiol.*, 1935, 3, 354.
16. LEIBOWITZ, S. L. Improved apparatus for determination of cholesterol. *J. Lab. & Clin. Med.*, 1935, 26, 857.
17. MACNIVEN, W. D. A consideration of the relative toxicity of uremic albumin for animals of different ages. *J. Exper. Med.*, 1935, 1, 7, 26.
18. MARPOT, M., and SATO, I. Ueber die allergische Gewebsreaktion der Niere. Zugleich eine experimentelle Beitrag zur Pathogenese der diffusen Glomerulonephritis und der Perinephritis nodosa. *Arch. f. path. Anat.*, 1934, 203, 65.
19. MICHAEL, R. D. and KEITH, V. M. Significance of nephritis of pregnancy. *J. Am. M. Ass.*, 1928, 9, 2044.
20. NEQUARTEN, L. Ueber das Schicksal der Kinder eklampsischer Mütter. *Zentralbl. f. Gynäk.*, 1925, 49, 913.
21. PAOL, L. H. The relationship of the extrinsic renal nerves to the origin of experimental hypertension. *Am. J. Physiol.*, 1935, 66.
22. PETTERSON, R. A critical review of 300 published and unpublished cases of abdominal cross-section for eclampsia. *Am. J. Obst.*, 1934, 69, 900.
23. RIMMO, R. H., JONSSON, A. L., and RICHARDS, E. T. A study of the action of alterable staphylococcal toxin on the kidneys of normal rabbits. *Am. J. Path.*, 1934, 475.

- 24 SMADEL, J E, and FARR, L E Experimental nephritis in rats induced by injection of anti-kidney serum II Clinical and functional studies J Exper Med, 1937, 65 527
- 25 STANDER, H. J William's Obstetrics, a Textbook for the Use of Students and Practitioners Chap 29 New York D Appleton Century Co, 1936
- 26 Idem The toxemias of pregnancy Medicine, 1929, 8 1
- 27 Idem. A new classification of the toxemias of pregnancy Am J Surg, 1940, 48 112
- 28 STANDER, H. J, and PECKHAM, C H A classification of the toxemias of the latter half of pregnancy Am J Obst & Gynec, 1926, 11 583
- 29 TEEL, H M, and REID, D E Eclampsia and its sequelæ, a clinical and follow-up study of all cases at Boston Lying In Hospital over a twenty year period Am J Obst & Gynec, 1937, 34 12
- 30 VAN SLYKE, D D, and CULLEN, G E A permanent preparation of urease and its use in the determination of urea J Biol Chem 1914, 19 211
- 31 VON JASCHKE, R. T Beitrag zur Klarung des Begriffes und zur Differentialdiagnose verschiedener Nieren erkrankungen in der Schwangerschaft Arch f Gynaek, 1921, 114 255
- 32 WOOD, J E, and CASH, J R Experimental hypertension—in sustained elevation of systolic and diastolic pressure J Clin Invest, 1936, 15 543

# NASAL SIMULTANEOUS GASTRODUODENAL ASPIRATOR

## Its Use in Postoperative Gastro-Intestinal and Abdominal Surgery

MOSES EINHORN M.D. New York, New York

THE nasal gastroduodenal aspirator finds application in many gastro-intestinal and abdominal surgical conditions, particularly in intestinal obstruction.

Intestinal obstruction is a condition in which fecal movement is prevented or impeded by either complete or partial occlusion of the bowel lumen. The primary cause is entirely mechanical and is due to a blocking of the lumen of the bowel from within or to compression from without, with the exception of those conditions which produce paralysis of the muscular wall of the bowel. This latter type which is known as the paralytic form, may be reflex or toxic due to inflammations, intestinal trauma, or shock.

Intestinal obstruction brings on a group of symptoms and signs, the most important of these being colic like intermittent pain, vomiting, and distention. Vomiting is an early and prominent symptom and usually projectile in character with the onset of obstruction. It comes on long before regurgitation of intestinal contents into the stomach takes place. If the obstruction is high, the damming back of digestive juices results in a regurgitant type of vomiting which is accompanied by nausea and is continuous whether or not food or fluid is given by mouth. True fecal vomiting is rarely observed.

On the other hand in low obstruction, vomiting is a late feature and may be absent throughout the course of the disease. Vomiting causes a loss of body fluids, dehydration and with it is associated a disturbance of the physicochemical balance manifested chiefly by the loss of sodium and chloride ions.

In low obstruction, the usual sign is distention. The sequence of events in the production of distention is as follows. At the site of the obstruction, the advance of fecal material is halted, thus producing a stasis. To overcome this stasis an increase in the intestinal

peristaltic action takes place along with an increased outpouring of secretions from the neighboring organs. With this added secretion there is an accumulation of gas, the source of which is essentially swallowed air also air that has diffused through the intestinal wall and gas that has formed from fermentation, putrefaction and decomposition of ingested foods.

In normal conditions, 90 per cent of this gas is absorbed and exhaled through the lungs, and the remainder is expelled by way of the rectum. In intestinal obstruction, however there occurs a decrease in, or an absence of the absorptive capacity of the intestinal mucosa which causes fluids and gases to accumulate above the point of obstruction, thus augmenting the intra intestinal pressure which then gives rise to distention. The nonabsorbable gases are usually methane, hydrogen nitrogen, and the tertiary amines, constituting the bulk of gases causing distention.

If this increased distention remains uncorrected for any length of time, vascular changes and necrosis of the bowel wall will inevitably result with the development of an ever-deepening toxemia.

In spite of the great advances made in medicine and surgery and notwithstanding the great progress made in our knowledge of that condition, and in our clinical observations, physical examination, and in the introduction of new methods, intestinal obstruction remains one of the most serious conditions confronting the profession, and while there has been a substantial decrease in its mortality the death rate still continues to be appalling.

The literature is replete with data gathered by surgeons from hospital records which show a high death rate from intestinal obstruction, the average being between 60 to 75 per cent. up to 1926.

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series of 3,269 cases, Arhurst's 69.3 per cent in 346 cases, and Lee and Downes' figures of 75 per cent. C. Jeff Miller, of the New Orleans Charity Hospital, found a gross mortality of 61 per cent in 343 cases of intestinal obstruction. A substantial decrease in the death rate is revealed in the later statistics of Moss of the same institution covering the period from 1930 to 1934 who found in a series of 340 cases a mortality of 31.7 per cent, or less than half of Miller's series. On the other hand, Boyce, continuing these studies and covering the period from 1933 to 1936, reported a slightly higher mortality of 36.3 per cent. Van Buren and Smith found that the mortality of acute cases in their hospital dropped from 66 per cent in the 5 year period from 1919 to 1924 to 29.6 per cent in 1932 to 1937. Burgess, of London, found that in the 1,042 cases of intestinal obstruction studied by him, 395 patients died, or a gross mortality of 37.9 per cent. North, of Philadelphia, collected his mortality statistics from a series in the literature totaling 1,625 cases including 200 patients of his own, of whom 425 died, or a gross mortality of 29.2 per cent.

This substantial lowering of the mortality, as revealed by the above data, was due to a number of factors, such as improved medical skill in diagnosing the condition, early operative intervention and the selection of the optimum time, since it became apparent that intestinal obstruction must be relieved before distention had progressed to such a degree that it would interfere with the blood supply of the bowel. Rehabilitation of the patient was found to be of prime importance and this was accomplished by the administration of fluids in the form of glucose solutions either subcutaneously or intravenously to overcome dehydration which reduces the nonprotein nitrogen of the blood, promotes diuresis and enhances the liver's detoxifying function. The induced hypochloremia was corrected by giving sodium chloride in sufficient amounts to raise the blood chloride level, thus increasing peristalsis and augmenting the tone of the bowel. Gastric lavage, before operation, removed a considerable amount of the protein disintegration products responsible for the production of the toxemia.

In addition to these factors, a major part in lowering the mortality from intestinal obstruction was played by decompression. The oldest method of decompression was that of blind puncture of the distended loops of the bowel by means of a needle or trocar. A more controlled method of decompression—enterostomy—has been practiced with greater success in the last 75 years.

The modern conception of the term decompression relates to the use of tubes introduced into the gastro-intestinal tract by way of the nasal or oral routes. This method of effecting relief of distention is, likewise, not new. Kussmaul and Cahn, in 1884, first used an elastic stomach tube for aspirating purposes and reported that such a form of treatment diminished the intra-abdominal pressure, reduced the size of the bowel proximal to the point of obstruction, and retarded violent peristalsis.

With the advent of the small calibered tube, gastric and duodenal drainage was greatly facilitated. Westermann, in 1910, reported the use of such tubes by the nasal route for continuous drainage in cases of ileus associated with peritonitis and stated that such a method of procedure was first used by Tannier in the year 1888.

Levin, in 1921, introduced a tipless gastro-duodenal catheter tube, suggesting the nasal route in place of the oral for introduction. The tube had a velvet edge at its terminal end, exactly like a urethral catheter, No. 14 to 16 French, with a few oval side openings at its end. He claimed that the employment of this nasal route in its introduction eliminated any discomfort or choking sensation on the part of the patient. The nasal route has not found much favor among gastro-enterologists in this country who contend that the oral method was far more preferable. They also claimed that for successful intubation of the duodenum the tube required weighting at its terminal end, so as to keep it in its proper place along the stomach pathway in its progress to the pylorus and to accelerate its entrance into the duodenum. The tube, in the course of the following few years, found its greatest application in surgery, and achieved its greatest popularity in postoperative drainage.



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Ward in 1925 advocated the use of gastric intubation with suction in the treatment of intestinal obstruction.

McIver and his co-workers, in 1926 used small calibered tubes as a prophylaxis in the postoperative treatment of ileus, demonstrating that the presence of gas was due largely to swallowed air.

For the past 20 years, Wangenstein has interested himself in the problems of intestinal obstruction engaging in extensive experimental studies, the results of which he has applied clinically. As a surgeon he has had the opportunity to operate in a number of obstructive intestinal cases, using the decompression method in all of them. His method of decompression consisted at first, in introducing an ordinary Levin nasal tube at the end of which was attached a suction siphonage apparatus. It soon became apparent however to Wangenstein and his co-workers that such a tube when placed in the stomach would not keep that viscous continuously empty and would be effective only intermittently as the stomach filled again. Moreover drainage of the duodenum could not be accomplished, except when there existed regurgitation of the duodenal contents back into the stomach, because the activity of the pyloric sphincter usually interrupts the continuity of the stomach and small intestines as a single tube. Besides, in order to accomplish a successful intubation of the duodenum for decompression, it was necessary to weight its terminal tip so as to accelerate its entrance through the pylorus into the duodenum. In order to obtain a successful decompression, they realized the necessity of siphoning both the contents of the stomach and duodenum at the same time.

Keeping these points in mind Wangenstein and his co-workers (17) modified the ordinary nasal tube by having the last 4 inches of the terminal end of the tube impregnated with lead to facilitate its entrance into the duodenum. They also increased the number of openings, placing 9 of them in the last 10 inches of the tube in the belief that, with the anchoring of the terminal end in the duodenum continuous suction siphonage could be executed simultaneously from the stomach

and from the upper reaches of the intestinal canal. Whether this could be really accomplished will be discussed later.

Intestinal decompression is a valuable preoperative measure in obstruction of the lower small bowel while preparations for surgery are being made. First, it allows gastric lavage which can be repeated until the return fluid is clear. Then the tube may be advanced further into the duodenum thereby removing accumulated liquid and gaseous material from the upper bowel and in this manner reducing or minimizing the degree of toxic resorption. Such decompression also obviates vomiting and prevents distention. It is of distinct advantage in that it decompresses the bowel gradually rather than abruptly and thus reduces the intraluminal pressure before irreparable damage is done, while, at the same time it permits the intestines and stomach to contract. By such means, the patient's general physical condition is improved and he becomes a better surgical risk; the surgeon may open the abdomen calmly and do the necessary surgery with assurance that the individual will pass through the ordeal without the danger of gangrene or rupture of the bowel.

After operation, decompression is of enormous value not only in relieving distention and in draining the bowel, but also in protecting it, as it were, until it can regain its normal tone. By keeping the stomach empty nausea and vomiting after operation are eliminated, the patient is comfortable, as proved by the figures of Wangenstein (17) who reduced the incidence of the symptoms by suction siphonage from 90 to 15 per cent. Decompression undoubtedly has added to the operative safety of the patient in acute intestinal obstruction and to his postoperative comfort.

Thus it is seen that decompression at times offers a means of relieving the patient's distention, without operation. This procedure makes it also possible to delay surgery safely until the patient's general condition is improved and his fluid and chemical balance becomes normal. Operation then becomes a procedure of election rather than one of emergency. The technical difficulties attendant

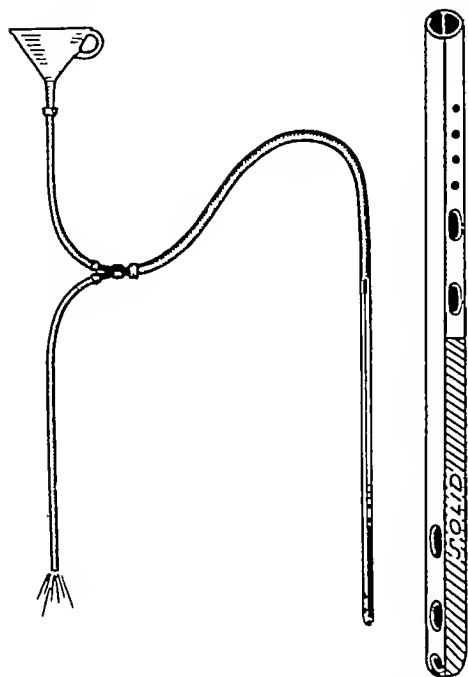


Fig 1 Author's double channel esophageal lavage tube

upon the operation on distended loops is removed

Soon after Wangenstein's enlightening contributions came the illuminating work of Abbott, Miller and Johnson (12). They designed a double lumen tube, the basic principle of which is the same as that which had for some time been used in colonic irrigations. The larger channel which serves as an aspirator, extends distally to the perforated tip attached to the end of the tube. The smaller channel serves as a passage for air for an inflation balloon placed at the terminal end. After the tube had passed the pylorus the balloon is inflated and peristalsis carries its end to the point of obstruction. They claim that their tube offers the possibility of extending the efficacy of suction-drainage by affording drainage at the bottom rather than at the top of a distended column of fluid and gas.

A detailed analysis of the advantages and disadvantages of this tube and its rôle in decompression will be in a separate paper describing the author's new intestinal aspirator.

Decompression can be used either as an adjunct to surgery before operation or after

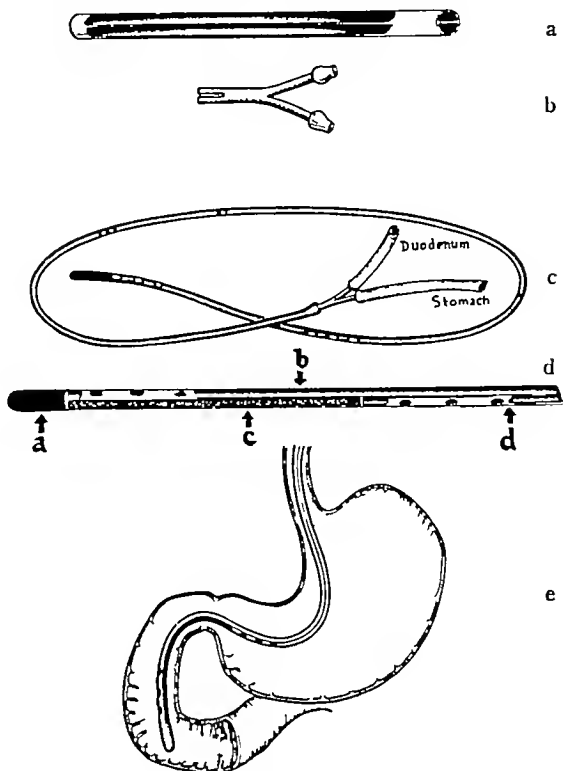


Fig 2 Author's nasal simultaneous gastroduodenal aspirator

operation, or, in some cases, can replace surgery entirely. This paper does not deal with the problem in which types of cases decompression should be used alone or as an adjunct to surgery—that is for the surgeon to decide. My concern here is to present a new tube which will achieve a most effective decompression.

In the course of my work in gastro-enterology, I felt the need for a tube that would make possible the obtaining of a simultaneous specimen from the stomach and duodenum. There are on the market a number of tubes for such a purpose and nearly all of them consist of a shorter tube fused or vulcanized to a longer tube and have at their end a metal bucket. Such a tube does not permit nasal intubation, and is too bulky even for oral introduction and too uncomfortable for retention by the patient for long periods of time.

In 1939, in my article on "The Treatment of Cardiospasm" (7), I described a double

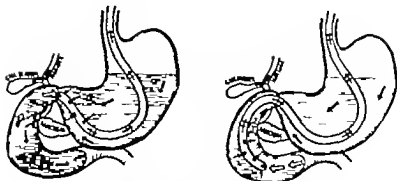


Fig. 3. The rôle of the Levin tube in decompression.

lumen tube for esophageal lavage (Fig. 1). The tube is No. 28 French, 30 inches in length and bisected into two distinct canals. One of the canals terminates at a point 4 inches short of the tip while the remainder of its lumen is filled with solid rubber. Immediately above this solid portion the walls feature a few wide openings. The second canal extends to the very end of the tube and has at its terminal end a few oval perforations. The idea occurred to the author that by incorporating this principle we would have a very simple simultaneous nasal gastroduodenal aspirator.

This tube (Fig. 2 c) is 50 inches in length, No. 16 French, semi-soft in consistency flexible, and of good resiliency. Its lumen is equally divided into two channels, semilunar in shape (Fig. 2 a) and terminates in a catheter-like tip which is made of solid lead impregnated rubber for a distance of  $3\frac{1}{4}$  inches (Fig. 2 da). The duodenal side (Fig. 2 db) of the double channel extends down to the solid rubber tip and has 3 oval openings slotted in appearance and  $\frac{1}{4}$  inch apart. The gastric side (Fig. 2 dc) of this double channel ends at a point about 7 inches above the solid rubber tip; the remainder of its lumen is filled with lead shot (Fig. 2 dd). Immediately above the lead filled portion there are 3 openings oval in shape and  $\frac{1}{4}$  inch apart.

The tube has a one ring mark placed at 19 inches, which represents the distance from the nares to the cardia; a two-ring mark at 30 inches which is the distance from the nares to the pylorus; and a three ring mark at 36 inches from the tip. This permits 6 inches of the terminal end of the tube to enter the

duodenum and leaves a space of 3 inches from the lower opening of the gastric channel. It is understood however that the physician's judgment should always determine the length of the tubing necessary for each individual, and he should not always rely entirely on the markings.

The special double channel connector (Fig. 2 b) consists of two narrow metal tubes soldered together in the middle and branching off distally into two separate canals, each of which is cemented into the proximal opening of the tube to render it airtight. Proximally the connector bifurcates into two channels, one representing the gastric outlet and the other the duodenal (Fig. 2 c).

Normally as it is well known, the duodenum receives the greatest flow of digestive secretions where the openings of the common and pancreatic ducts are located. These secretions are mixed with the products of gastric digestion and pass into the small intestine where the final stage of digestion takes place. The greatest portion of the products of digestion is absorbed in the intestines and the remainder travels on to the colon.

However in intestinal obstruction the advance of fecal material is halted, and a stasis of the accumulating food material is produced. To overcome this condition, there is an increased intestinal peristalsis together with a compensatory increase in secretion from the neighboring organs and gut. The intestines receive an increased volume of fluid material together with the accumulated gas, which is essentially swallowed air and the end products of fermentation and putrefaction.

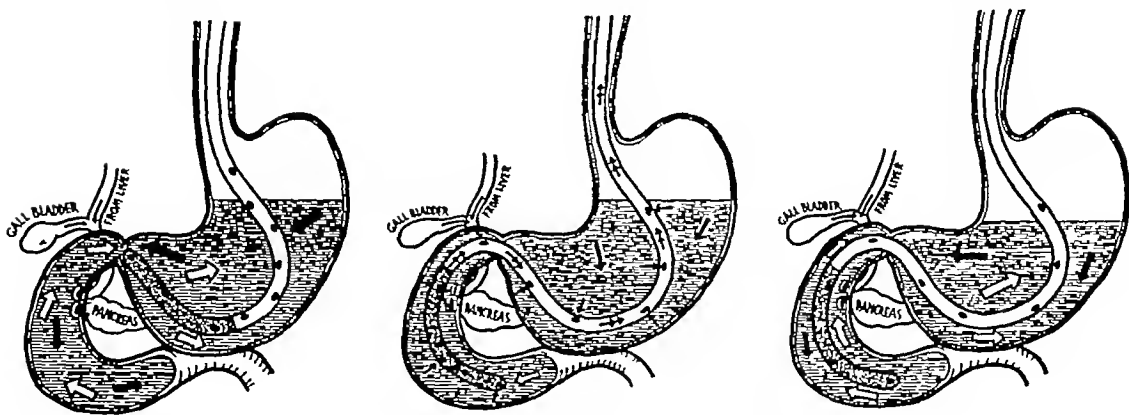


Fig 4 The rôle of Wangensteen tube in decompression

There occurs, at the same time, a decrease or absence of the absorptive capacity of the intestinal mucosa. This acts as a contributory cause of accumulation above the point of obstruction and augments the intra-enteric pressure that gives rise to distention. As soon as this column of accumulated material extends to the higher reaches of the duodenum, there is a retroregurgitation through the pylorus into the stomach with subsequent vomiting.

In order to eliminate vomiting associated with intestinal obstruction, surgeons and clinicians have employed siphonage by means of small calibered tubes introduced through the nose, particularly the Levin tube.

To understand the exact rôle that each of the tubes plays in siphonage, I have prepared a set of diagrams which clearly illustrate what each tube actually accomplishes in bringing about decompression.

#### THE RÔLE OF THE VARIOUS TUBES IN DECOMPRESSION

Let us now proceed to the evaluation of the principal tubes that lend themselves to application in drainage of the stomach and duodenum.

*The Levin tube.* This tube has four openings at its terminal  $2\frac{1}{2}$  to 3 inches. When propelled forward, and on reaching the fundus of the stomach, it will permit the sucking out of gas bubbles by the application of a suction siphon. In its further progress within the stomach the Levin tube will remove all the accumulated fluid. This is shown in the ac-

companying diagram (Fig 3, a, left) by the black arrows pointing toward the openings. The double arrows show the direction of the aspirated fluid within the tube on its way out.

It will be seen, however, that the Levin tube, being a single tube, will not simultaneously drain any duodenal contents except those that enter the stomach from time to time by way of regurgitation as shown by the white arrows. It will only drain the duodenal contents alone when it enters that part of the gut. Parenthetically, it may be remarked here that the Levin tube, not being weighted, is not very efficient in reaching the duodenum with speed and promptness. Most gastroenterologists agree that weighting *does* promote and accelerate the transit of a drainage tube into the duodenum. The absence of weighting detracts markedly from that function of the tube.

Now let us assume that the Levin tube has entered the duodenum in the course of its progress. Drainage then takes place through it, as shown in diagram (Fig 3, b, right). The drainage fluid in the duodenum consists of biliary and pancreatic secretions, besides its own, and regurgitated fluid from the jejunum, as shown by the white arrows. However, nothing can be drained from the stomach at the same time, neither gas nor fluid, save that which has passed through the pylorus into the duodenum during normal peristalsis. Thus no combined gastric and duodenal drainage is possible through the Levin tube.

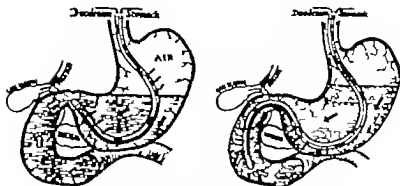


Fig. 5. The rôle of author's tube in decompression.

**Wangenstein tube** This tube is claimed by its proponent to give a very efficient performance in actual drainage and decompression of the stomach and duodenum. Wangenstein states that his tube, when placed in the stomach, is capable of withdrawing all the fluid and gas in that viscus. When the tube is in the duodenum he claims that it provides a continuous and simultaneous withdrawal of liquid and gas from both stomach and duodenum.

*How true is that claim?*

On actual testing of that tube *in vitro* these desired results are unfortunately not obtained, as any one can convince himself by actual experiment. The reason for this failure is as follows. It will be recalled that the Wangenstein tube has 9 openings in its terminal 10 inches. However the usual measurements of the average normal stomach from cardia to pylorus is 11 inches. All the duodenal tubes are marked in accordance with this fact. The distance from the nose to the cardia is 19 inches, from nose to pylorus, 30 inches. Let us suppose that the Wangenstein tube has been introduced up to the 30 inch mark. This should bring the tube right to the pylorus and should leave its entire terminal 10 inches in the stomach. On actual drainage however very little comes out except a little air or the gas bubble. The reason is that *no fluid will drain out if any of the openings are placed above the fluid level*. Because of the many widely spaced openings in the terminal portion of that tube it suffices that only one of these openings be above the fluid

level to prevent any drainage of fluid through it. This is a well recognized and old established physical law.

On accompanying diagram (Fig. 4, a, left) this is indicated by the absence of double arrows from the tube showing no drainage stream within it. If through regurgitation from the duodenum fluid accumulates in the stomach so as to raise its level above the highest opening, drainage will take place only so long as that highest opening is below the level of the fluid. Should sufficient fluid be drained off to cause the highest opening of the tube to emerge above the fluid level, *drainage will immediately cease*.

When the Wangenstein tube advances into the duodenum i. e. to the final 32 inch mark, its final 4 inches lying in that viscus *under* the fluid level, and the upper openings being in the stomach *below* its fluid level, *then and only then* will simultaneous drainage from both duodenum and stomach take place. This is indicated in the diagram (Fig. 4, b, center) by the black arrows. The white arrows show the regurgitation from the jejunum into the duodenum the double arrows show as before the direction of the stream of drainage within the tube.

However no sooner does the level of the fluid within the stomach drop and the upper most openings emerge above the fluid level then drainage promptly stops. This is indicated in the diagram (Fig. 4 c, right) by the absence of double arrows within the tube.

Now let us imagine that most of the openings of that tube are in the duodenum and

that some are in the stomach and that full emptying of the stomach has taken place. As soon as one opening within the stomach emerges above its fluid level, then no fluid can be drained from the duodenum, in spite of the fact that most of the openings of the tube are within it. In other words, the fluid is trapped within the duodenum.

*In vivo* this law, as outlined above, holds too. However, we must admit that when used on the living patient we may often achieve a partial drainage with the Wangensteen tube in the normal or hypertonic individual. This is due to a number of factors that cause a narrowing of the contour of the stomach and a consequent rise of its fluid contents above the uppermost opening on the tube. These factors are: active peristalsis, a good muscular tone, good diaphragmatic action, deep respiration, etc. However, complete drainage is *never* achieved. This I was able to verify by barium studies on patients through the fluoroscope.

But in the pathological conditions of the stomach, such that cause atony or dilatation, in pyloric or intestinal obstruction from any cause and other similar factors, drainage through the Wangensteen tube will depend upon whether the upper openings are below the fluid level.

*Author's tube* My own double tube for simultaneous gastric and duodenal drainage is designed to overcome this defect of the Wangensteen tube. In the first place, my tube has two independent channels, one, the lower channel—the duodenal side—has 3 openings in its final  $1\frac{1}{2}$  to 2 inches. The upper channel—the stomach side—is placed  $9\frac{1}{2}$  inches from the terminal tip of the tube. It has likewise 3 openings which extend for  $1\frac{1}{2}$  inches. This channel represents the gastric side.

When this tube is passed to the fundus of the stomach it will immediately remove the air of the gas bubble. On further advance within the stomach, as soon as its terminal 2 inches are submerged below its fluid level, effective suction—drainage will be established. In its progress to the pylorus the weighted tip helps the tube to keep its position and direction within the stomach pathway, while it

continues suction all the time. On reaching the pylorus this tube will have effectively removed all the stomach contents, the lower openings draining the fluid, the uppermost, the air at the same time (Fig 5, a, left).

When the tube passes the pylorus and all the lower openings are in the duodenum (as seen by the three-ring mark of  $36\frac{1}{2}$  inches from the terminal tip) the duodenal contents begin to be drained. This includes, of course, also the regurgitated fluid from the jejunum. In the diagram the black arrows show the direction of the fluid from the jejunum, while the double arrows show the direction of the drainage fluid within either channel of the tube.

The additional accumulation of fluid and air within the stomach is simultaneously taken in hand by the gastric portion of the tube. Even when the stomach has been entirely emptied, the duodenal side will still continue to drain out both the pancreatic and biliary flow and the regurgitated fluid from the jejunum, the reason being the separate channel allotted to this drainage, independently of the stomach.

#### THE USE OF THE DOUBLE TUBE IN GASTRO-ENTEROSTOMY

When Levin introduced his nasal tipless catheter tube in 1921, he suggested that before closing the abdomen, the surgeon could pull the tube through the gastro-enterostomy opening and in that way introduce fluids into the duodenum or jejunum after the operation.

Abbott and Rawson (1, 2) in 1937, described another type of tube for use in patients undergoing gastric operations. The purpose was twofold: first, to keep the stomach constantly empty, and, second, to allow jejunal feeding at regular intervals. This was accomplished by the insertion of a silver outlet valve into a regular duodenal tube at the tip for jejunal feeding and of a silver inlet valve, 30 centimeters proximal to the tip, for the aspiration of gastric contents. This one lumen, valved tube was soon abandoned by Abbott and Rawson who found it inadequate and in 1939 they substituted (2) a 2 lumina tube. This tube is 130 centimeters in length, 100 centimeters of which has two lumina, No. 16 French, and is joined by a metal connector to



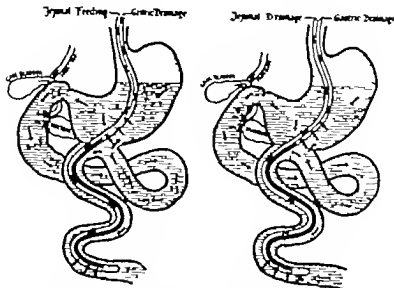


Fig. 6. The use of author's tube in gastro-enterostomy

a one lumen strip 30 centimeters in length and No. 12 French. Above the metal connector are five openings which represent the gastric side and at the end of the one lumen tube is a metal bucket which represents the jejunal outlet. Markings are placed at a distance of 75 and 85 centimeters from the bucket. The tube is introduced in the following manner. It is passed through the nose, the end is drawn out of the mouth and a metal bucket is attached. The patient is then instructed to swallow the tube to the first mark which is 75 centimeters from the bucket of the tube. When gastro-enterostomy is performed, the surgeon on completion of the anastomosis, slips the bucket of the tube with his thumb and fingers till it lies 30 centimeters down in the efferent jejunal loop. The tube meanwhile is advanced until the 85 centimeter mark reaches the external nares and is retained in that position. Six hours after operation nutrient solution may be introduced through one side of the tube which connects with the tip while through the small openings which lie in the stomach, drainage can be carried out. To remove the tube the tip must be withdrawn through the mouth the bucket removed and the tube then replaced in the mouth and withdrawn through the nose.

The procedure just described is obviously impractical. To overcome these defects, I have modified my double channel tube for possible use in cases of gastro-enterostomy by raising its upper openings to 12 inches from the solid lead impregnated rubber tip, at the same time lengthening the lead shot compartment. The one ring mark is placed at 30 inches and the two ring mark at 37 inches. The tube is inserted through the nose in the ordinary way up to the one ring mark, thus allowing 12 inches to remain in the stomach. On completion of the anastomosis the surgeon slips the terminal end of the tube down into the efferent jejunal loop for a distance of about 14  $\frac{1}{2}$  inches or until the two ring mark reaches the external nares. In this manner the uppermost opening will lodge in the stomach for gastric drainage while feedings can be supplied to the jejunum through the lower openings (Fig. 6 a, left). A drainage from both stomach and jejunum could be obtained (Fig. 6 b right). When this tube is ready for removal it can be withdrawn in the ordinary way through the nose.

#### TECHNIQUE FOR NASAL INTUBATION

The terminal end of the tube which has previously been dipped in glycerin, is intro-

duced through the nose for a distance of 6 inches, and the patient is then asked to simulate the act of swallowing, while the operator pushes the tube which will be carried down slowly in the esophagus because of its lead weight compartment

As soon as the first ring mark is reached the patient is turned on the right side. The patient is instructed to swallow the tube very slowly, an inch at a time, over a period of 20 to 25 minutes, until the third ring mark is reached, so that the terminal end will enter the duodenum

*Tests for determining the entrance of the terminal tip into the duodenum* 1 Fluoroscopic and x-ray examinations are of aid in determining the entrance of the tip into the duodenum. Although this method is undoubtedly reliable, yet I believe that it should not be used in routine practice, since in the course of removing the patient to the x-ray room and by manipulation, the terminal portion of the tube may easily slip back into the stomach even with the lead weighted tip

2 Observation of the differences in color, viscosity, and reaction of specimens obtained from the two outlets: the duodenal specimen will be viscid, golden yellow in color, and negative to Congo red, whereas the gastric specimen will be clearer, perhaps bile-tinged, but positive to Congo red

3 Injection of a mixture of barium or any other colored solution into the duodenal outlet, no return of dye on the gastric side indicates that the terminal tip has entered the duodenum

#### USES

The method has been of use in the following cases

1 In pre-operative and postoperative gastro-intestinal and abdominal surgery when simultaneous and continuous gastro-intestinal drainage (S) is wanted

2 In cases in which tubal feeding and drainage are required

3 In cases of gastro-enterostomy

4 The use of the tube in medical cases will be presented in a separate paper

#### ADVANTAGES

The tube has the following advantages

1 Effective decompression by means of simultaneous gastroduodenal drainage is offered only through this tube

2 In gastro-enterostomy cases, jejunal feeding and gastric drainage are easily accomplished without the use of any buckets

3 The 1½ inch solid lead impregnated rubber tip at the terminal end facilitates introduction and passage of tube through the nares

4 The weight of the lead-shot compartment together with the lead impregnated rubber tip facilitates the passage of the tube through the esophagus, maintains it in its proper position along the stomach pathway, and aids its entrance into the duodenum

5 There is less possibility of the lower part of the tube regurgitating into the stomach, as the weight of the lead impregnated solid portion and the lead shot compartment keeps it securely in the duodenum

I wish to express my gratitude to Mr. L. T. Hilborn, president of Clay-Adams Co., for his kind co-operation in the development of the tube

#### BIBLIOGRAPHY

- 1 ABBOTT, W. O., and RAWSON, A. J. *J. Am. M. Ass.*, 1937, 108: 1873
- 2 Ibid, 1939, 112: 2414
- 3 BEST, P. W. *J. Med. Ass. Georgia*, 1925, 14: 192-195
- 4 BOYCE, F. T., and MCFETRIDGE. *South Surgeon*, 1937, 6: 109-125
- 5 BURGESS, A. H. *Lancet*, 1929, 1: 857
- 6 EINHORN, MOSES. *Am. J. Digest. Dis.*, 1938, 5: 77-80
- 7 Idem. *Rev. of Gastroenterol.*, 1939, 6: 499
- 8 KUSSMAUL and CAHN. *Berl. klin. Wchnschr.*, 1884, 21: 1669-1685
- 9 LEVIN, A. J. *J. Am. M. Ass.*, 1921, 76: 1007
- 10 McIVER, M. A. et al. *Arch. Surg.*, 1926, 13: 588
- 11 MILLER, C. JEFF. *Ann. Surg.*, 1929, 89: 91
- 12 MILLER, T. G., and ABBOTT, W. O. *Am. J. M. Sc.*, 1934, 187: 595-600
- 13 MOSS, W., and MCFETRIDGE, E. M. *Ann. Surg.*, 1934, 100: 158-166
- 14 NORTH, J. P. *Internat. Clin.*, 1929, series 39, 3: 206
- 15 VAN BUREN, F. T., and SMITH, B. S. *Arch. Surg.*, 1927, 15: 288-297
- 16 WANGENSTEEN, O. H., and PAINE, J. R. *J. Am. M. Ass.*, 1933, 101: 1532
- 17 Idem. *Minnesota Med.*, 1933, 16: 96
- 18 WARD, R. *J. Am. M. Ass.*, 1925, 84: 114
- 19 WESTERMANN, C. W. *J. Zentralbl. f. Chir.*, 1910, 37: 356

# THE OBSTETRIC EXPERIENCES OF WOMEN PARALYZED BY ACUTE ANTERIOR POLIOMYELITIS

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THE primary purpose of our investigation was to determine the effect of paralysis due to acute anterior poliomyelitis on the course of pregnancy and labor. Information was gathered concerning 243 paralyzed women who had had one or more pregnancies subsequent to the onset of the paralysis. We examined 44 of this group of cases personally at the Hospital for Joint Diseases, and we studied the 199 remaining cases through questionnaires which were filled out by the attending obstetricians and orthopedic surgeons and in some instances by the patients themselves. We have been fortunate in obtaining the co-operation of many physicians throughout the United States, and we are indeed grateful to them. The questionnaires are lengthy and comprehensive copies of them will be found in our original report to the Foundation. Our investigation also afforded us the opportunity of collecting 13 cases in which pregnancy was complicated by an acute attack of anterior poliomyelitis. In addition we studied the structure of the pelvis of 101 paralyzed women of whom 34 were married and 67 were single, by the Thomas "grid method of pelviroentgenography. This consists of x raying the patient's pelvis in a semi-sitting position and then, by the use of a calibrated grid placed in the same plane as that previously held by the pelvic inlet to superimpose a centimeter calibration on the roentgenogram thus permitting accurate measurements of the various diameters of the pelvic inlet. Our findings may be grouped under the following three studies: (1) Roentgenographic study of the pelvis of women previously paralyzed by acute anterior poliomyelitis. (2) pregnancy complicated by

an acute attack of anterior poliomyelitis. (3) pregnancy following previous acute anterior poliomyelitis.

## ROENTGENOGRAPHIC STUDY OF THE PELVES OF WOMEN PREVIOUSLY PARALYZED BY ACUTE ANTERIOR POLIOMYELITIS

Classifications of pelvic types have in the past been based largely upon anatomical specimens. It had become increasingly apparent, however, that such classifications were not of much value in guiding one as to the likely course of labor in a given case. In addition, obstetricians have learned that external measurements of the pelvis yield only an approximate and usually far from accurate estimate of the exact shape and size of the interior of the pelvis. The need for and many of the advantages of an exact knowledge of the structure of the pelvis have led to many studies in roentgenography of the female pelvis and roentgen pelvimetry. These studies have demonstrated that normal pelvis differ considerably in their morphology and that depending upon such differences, there are variations in the type of engagement of the presenting part and in the mechanism of labor. The roentgenographic study of the pelvis has been limited by some workers, as Thomas and Jarcho, to an analysis of the pelvic inlet as being sufficient for practical purposes, while others, notably Caldwell and Moloy, have made a more precise study of the pelvic interior through stereoscopic roentgenography.

We roentgenographed 101 paralytic females. There was some degree of asymmetry in 70.21 per cent while in 20.8 per cent the pelvic inlets were symmetrical (Table I). It is noteworthy that in a study of normal or unparalyzed women Caldwell, Moloy and Desopo found but 4 asymmetrical pelvis in 215 primigravidae. While the incidence of asymmetrical or deformed pelvis in infantile

The study was conducted at the Hospital for Joint Diseases, of New York City aided by a grant approved by The Committee on Research for the Prevention and Treatment of After Effects of The National Foundation for Infantile Paralysis, Inc.

Read before the American Orthopaedic Association, May 7

TABLE I—RELATION OF VARIOUS FACTORS TO  
ASYMMETRY OF PELVIC INLET  
In 101 Unselected Adult Paralytic Females

		Asymmetrical pelvis— 80 cases 79.21%	Symmetrical pelvis— 21 cases 20.79%
a Shortening of one lower extremity—99 cases 80.1%	Same side as flattening	38	15
	Side opposite flattening	17	
	No shortening—11 cases 10.9%	5	6
b Pelvifemoral muscle paralysis—77 cases 76.4%	Same side as flattening	5	5
	Side opposite flattening	22	
	Bilateral and equal	9	5
c Paralysis of muscles below hip—97 cases 96.2%	Same side as flattening	35	13
	Side opposite flattening	24	
	Bilateral and equal	15	7
d Axis deviation (rotation) 94 cases 92.1%	Toward side of flattening	51	16
	Away from side of flattening	6	
	No axis deviation 5 cases 5.0%	3	5

paralysis was very high we noted that the degree of contraction or flattening of the pelvis was generally slight and only exceptionally marked.

In an attempt to determine the forces which were influential in causing such pelvic deformation, we considered the following factors: (1) the effect of associated lumbosacral scoliosis, (2) the rôle of weight-bearing, especially as this factor might be influenced by the use of external appliances and various orthopedic reconstructive operations, (3) shortening of a lower limb, (4) muscle imbalance due especially to paralysis of the pelvifemoral and pelvispinal muscles, and (5) paralysis of the muscles below the hip.

1. *The effect of associated lumbosacral scoliosis (Tables I and II)* It has long been known that fixed lateral curvature of the spine is invariably associated with rotation of the vertebral segments toward the convex side and that in the dorsal region the ribs become deformed in such a way that there is flattening of the chest on the side of the convexity,

TABLE II—RELATION OF VARIOUS FACTORS TO  
AXIS DEVIATION (ROTATION)  
In 101 Unselected Adult Paralytic Females

		Axis deviation 31 cases 100%		No axis deviation
		right	left	
a Shortening of lower extremity	Same side	28	0	R 3 L 3
	Opposite side	18	0	
	No shortening	6	3	
b Pelvifemoral muscle paralysis	Same side	0	23	R 1 L 1
	Opposite side	1	6	
	Bilateral and equal	6	6	2
No pelvifemoral muscle paralysis		13	7	4
c Abdominal (anterior and lateral) and quadratus lumborum muscle paralysis	Same side	11		
	Opposite side	3		
	Bilateral and equal	6		
No paralysis of abdominal or quadratus lumborum muscles		73		8
d Relation of lumbosacral rotary lateral scoliosis	Group I (X-ray study)	Scoliosis present—30 cases 96.8%	Same side 17	13
		No scoliosis 1 case 3.2%	Opposite side	
	Group B (No X-ray study)	Scoliosis present	Same side 0	1
		No scoliosis present	Opposite side 3	1
			0	12
				8

anteriorly, and on the side of the concavity, posteriorly. We have anticipated that a like mechanism might be operative in the pelvis, by considering the innominate bones as representing the costal cage, the sacro-iliac joints as representing the costovertebral joints, and the symphysis pubis as equivalent to the sternocostal articulations. With a scoliosis involving the lumbar spine and sacrum and with rotation toward the convexity, one should, therefore, anticipate the following deformity of the pelvic ring—flattening anteriorly on the side of the convexity of the lumbosacral curve and flattening posteriorly on the side of the concavity (Fig 1). The effect on the costal cage by the rhythmic alterations of intrathoracic pressure consequent upon cardiovascular and respiratory functions is duplicated by the change in th

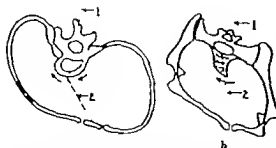


Fig. 3. a, Deformity of the costal cage secondary to rotary lateral scoliosis in the dorsal spine. There is flattening anteriorly on the side of the concavity of the dorsal scoliosis and flattening posteriorly on the side of the convexity. Sagittal axis of the thoracic vertebrae indicating rotation to the right. anteroposterior axis of the costal cage. b, Deformity of the pelvic ring secondary to rotary lateral scoliosis in the lumbosacral spine. There is flattening of the pelvic ring anteriorly on the side of the convexity and flattening posteriorly on the side of the concavity of the lumbosacral scoliosis. Sagittal axis of the sacrum indicating rotation to the right. anteroposterior axis of the pelvic inlet.

pelvic frame arising from the intra-abdominal pressure changes secondary to diaphragmatic movements and cardiovascular function. In 30 roentgenographically proved cases of lumbosacral scoliosis in this group there was in every instance the anticipated distortion and asymmetry of the pelvis (Table II). It may here be emphasized that the clinical judgment as to the presence, type and extent of a scoliosis, especially in the lumbosacral region cannot alone be relied upon and that a roentgenogram of the spine is essential for accuracy.

The anteroposterior axis of the pelvic inlet extends between the symphysis pubis and the sacral promontory. A shift of the sacral promontory to the right or left necessarily implies a shift or rotation of the anteroposterior axis of the pelvis. We found that in 93 of the 101 pelvic inlets there was deviation of the anteroposterior axis posteriorly to the right or to the left of the sagittal plane. In 51 cases there was asymmetry of the pelvis due to flattening anteriorly on the side corresponding to the posterior shift of the anteroposterior axis rotation (Fig. 3). In 16 cases with axis rotation, there was no asymmetry of the pelvis. Possibly the explanation of the absence of asymmetry in this group of 16 cases lies in the fact that not enough time had elapsed to

permit the change in the pelvic ring. In 20 cases there was asymmetry of the pelvis but the flattening was on the opposite side (Table I). It is difficult to explain the opposite sides of the axis deviation and flattening of the pelvis in these 26 cases unless it be that the flattening occurred on the same side as the original scoliosis, but that with the subsequent development of a lower compensatory curve the side of the axis deviation and the flattening have become oppositely placed. However in most of the cases there is apparently a definite relation between the rotation in the lumbosacral region arising from a lumbosacral scoliosis primary or secondary and the asymmetrical flattening of the pelvic ring (Fig. 3).

This relationship between lumbosacral scoliosis and asymmetry of the pelvis was further confirmed by roentgenography of the pelvic inlets of 4 cases of idiopathic scoliosis with lumbosacral curves, selected from a series of approximately 24 cases of idiopathic scoliosis. In these cases also the pelvic inlet was flattened anteriorly on the side of the convexity and posteriorly on the side of the concavity of the lumbosacral rotary-lateral scoliosis.

2. *The effect of weight-bearing on pelvic asymmetry.* Our studies lead us to believe that when weight is unequally distributed on the two sides of the pelvis the side on which there is greater weight and pressure will become flattened. In bedridden patient we find large symmetrical pelves. Similarly in those patients who walk with the aid of crutches and bear little or no weight on their legs, the pelvis remain large and fairly symmetrical (Figs. 4a and 4b). In 8 cases of paralytic dislocation of the hip we noted flattening of the pelvic inlet anteriorly on the side opposite the dislocation that is, on the normal or less paralyzed side. Due to the dislocation the direct thrust of weight bearing was brought to bear almost entirely on the side where no dislocation was present (Fig. 5). An additional experience was afforded in 3 cases with unilateral congenital dislocation of the hip in which there was paralysis following acute anterior poliomyelitis. In 2 cases flattening of the pelvic inlet occurred anteriorly



Fig 2 Pelvic inlet of a normal married female, nullipara, aged 27 years. There is perfect symmetry of both halves of the pelvis and of the pelvic inlet outline. *a*, sacral promontory, *b*, ischial spine, *c*, symphysis pubis. The anteroposterior diameter of the pelvic inlet equals 12.25 centimeters, transverse diameter equals 12.35 centimeters. Morphological classification of the type of pelvis: gynecoid type (Caldwell-Moley), average, round type (Thoms).

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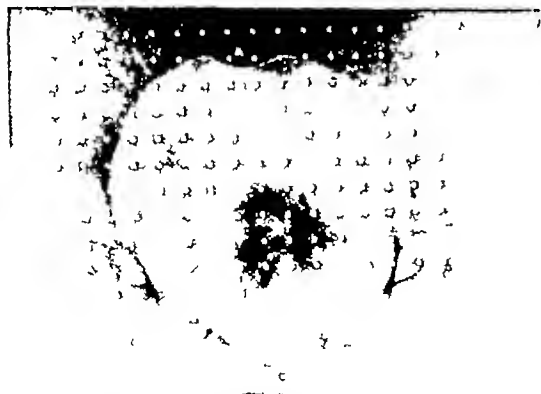


Fig 4a. This figure shows the effect of scoliosis without weight bearing. This is a case in which there was no weight bearing, the patient bearing most of her weight on her upper torso by means of two crutches. Photograph illustrates a large pelvic inlet with slight flattening of the right pelvis, anteriorly, and slight anteroposterior axis rotation to the right, posteriorly. *a*, Sacral promontory, *c*, symphysis pubis. Arrow marks slight flattening of the pelvic inlet on the right side anteriorly. This patient is 20 years old, single and has been paralyzed for 10 years. There is severe involvement of both lower extremities which are flail, but there is no shortening. There is a right lumbar, right lumbosacral scoliosis. X-ray measurements: anteroposterior, 11.65 centimeters, transverse, 11.75 centimeters.

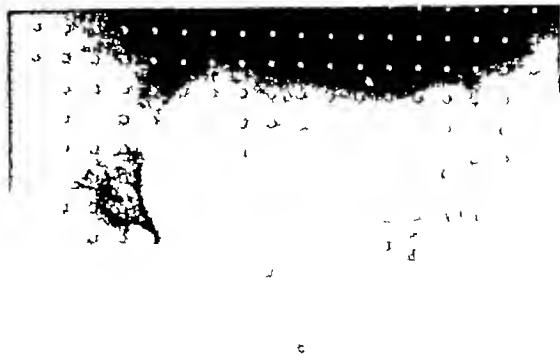


Fig 3. There is flattening of the pelvis anteriorly on both sides, more marked on the left, secondary to a left lumbar, left lumbosacral scoliosis. There is anteroposterior axis rotation of the pelvic inlet to the left posteriorly. *a*, Sacral promontory, *b*, ischial spine, *c*, symphysis pubis, *d*, obturator foramen. This patient is 24 years old, single and has been paralyzed for 23 years. There is complete paralysis of both lower extremities without shortening. She wears two long leg braces and utilizes no crutches. X-ray measurements: anteroposterior, 7.75 centimeters, transverse, 11.25 centimeters.

curred on this side because the lesser trochanter abutted satisfactorily upon the acetabulum, permitting stable weight bearing (Fig 7). Thus, we conclude that weight-bearing is an important factor in poliomyelitis in causing or contributing toward flattening

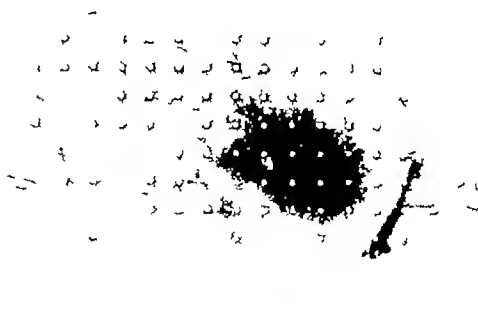


Fig 4b. This figure shows the effect of weight bearing without scoliosis. In this case there was symmetrical flattening of both sides of the pelvis, anteriorly, with shortening of the anteroposterior diameter of the pelvic inlet and without axis rotation. *a*, Sacral promontory, *c*, symphysis pubis. This deformity was secondary to weight bearing by means of two long leg braces without the aid of crutches, both lower extremities being flail. There was no shortening or scoliosis. X-ray measurements: anteroposterior, 7.30 centimeters, transverse, 12 centimeters.

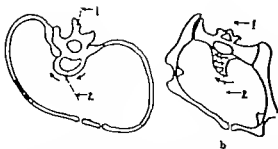


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This relationship between lumbosacral and asymmetry of the pelvis is confirmed by roentgenography of inlets of 4 cases of idiopathic scoliosis and lumbosacral curves selected from approximately 24 cases of idiopathic scoliosis. In these cases also the pelvis flattened anteriorly on the side of convexity and posteriorly on the side of concavity of the lumbosacral scoliosis.

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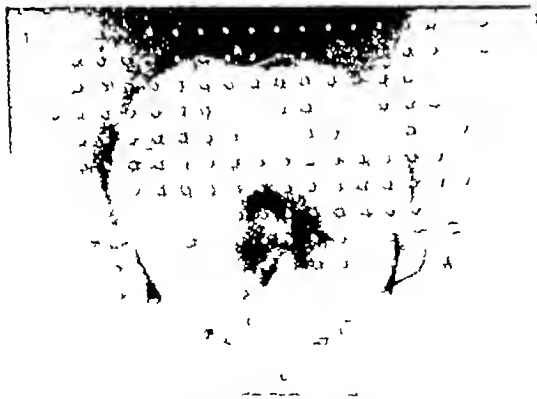


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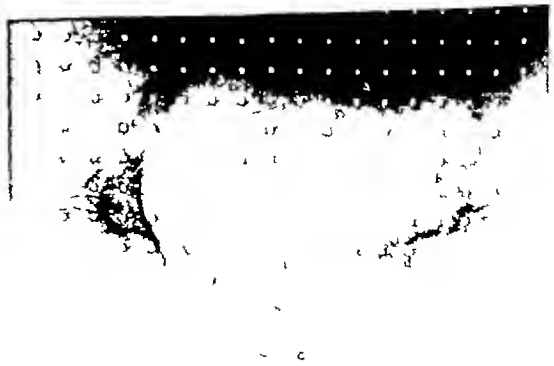


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TABLE III — ORTHOPEDIC STATUS IN 209 CASES  
(GROUPS A—D\*)

Extent of paraly- sis	% of cases	Incidence percentage per group
One or both lower extremities	34	50.31
One or both upper and lower extrem- ity	6	8.7
One or both upper extremities	5	3.0
Abdomen or back muscles	5	3.0
Abdomen, back, and extremities	5	9.0
Inadequate data	44	66
Deformities		
None	41	61
Deformities of trunk and/or ex- tremities	40	66.98
Inadequate data	3	
External appliances		
None	15	64.57
Brace, corset and/or crutches	60	33
Inadequate data	5	40
Orthopedic operations		
None	84	40.9
Stabilizations, tendon transplants and/or correction deformities	96	45.5
Inadequate data	29	6.73

\* (Group A—cases delivered with ease.

\* (Group B—cases delivered with difficulty

TABLE IV — AGE DURATION OF POLIOMYELITIS  
NUMBER OF YEARS MARRIED NUMBER OF  
PREGNANCIES AND DELIVERIES (GROUPS A  
AND B)

Present age (age years)		Duration of poli- omyelitis prior to first pregnancy (year cases)		Number of years married prior to first pregnancy (year cases)	
Age (years)	No. of cases	No. of years	No. of cases	No. of years	No. of cases
10-15		0-11 years			24, 27.6%
16-20			779	10	
21-25	41	0-10			21
26-30	64, 30.6%		37		
31-35	42	10-20	14, 34.3%		
36-40	10	20-25	24, 24.0%		
41 years		26-30	17		
Unknown		1-5	3		
		31-35		2-4	
		Unknown		Unknown	24
Pregnancy—1-10 years					
Obstet—1-30 years					
Delivery—1-30 years					

Number of pregnancies (age years)			Number of deliveries (year cases)		
No. of pregnancies per case	No. of cases	Total No. of preg- nancies	No. of deliveries per case	No. of cases	Total No. of deliveries
100, 30.6%	100		17	17	17
15, 4.5%	20		20, 24.0%	20	20
25, 6.2%	92		21, 20.0%	21	21
	64				24
	30				24
	8				24
	12				21
100	10	100			24
100	61				21
Maximum number of preg- nancies per case			Maximum number of deliv- eries per case		
Maximum number of preg- nancies per case			Maximum number of deliv- eries per case		
			Number of abortions		

\* Group A—cases delivered with ease.

\* Group B—cases delivered with difficulty.

\* Excluding 3 cases who were pregnant at time last analysis was completed, of whom were pregnant, and 10 cases previously unreported.

months. The age of the mothers varied from 17 to 28 years. There were normal spontaneous deliveries in 5 cases a breech extraction in 1 case, while in 4 instances forceps were employed after the head had spontaneously descended to the pelvic floor. There were 2 difficult mid forceps deliveries with birth of normal children. A spontaneous miscarriage occurred in 1 instance 1 week after the acute attack. A normal child was obtained in the 12 patients who delivered at term.

From the preceding résumé it becomes apparent that notwithstanding severe paralysis involving the abdominal and extremity muscles and occurring during gestation a normal course of pregnancy and labor and a normal offspring may be anticipated. The reason for this is premised not only upon the clinical facts as obtained in the cases here noted but also upon experimental evidence. Physiologists have demonstrated that the uterus will contract after division, not only of the spinal cord but also of its sympathetic nerve supply proving that the uterus has an independent nerve supply within its own substance which is not disturbed by anterior poliomyelitis. A like experience has been noted in patients paralyzed following cord

tumor spondylitis, and vertebral fracture. It is true that after the presenting part has

descended spontaneously to the pelvic floor the absence of adjutant voluntary powers may necessitate the employment of some mechanical maneuver, such as manual extraction or forceps, to effect completely the delivery, but this does not constitute a danger to either the mother or child

The appearance of acute anterior poliomyelitis during pregnancy, therefore, need not cause undue alarm. Except in the rare instances of bulbar or ascending paralysis, there will not be a fatal issue but rather progressive improvement or recession of the paralysis after the usually short acute stage has passed. One should not contemplate a therapeutic abortion as the senior author advised several years ago from sheer ignorance. The pregnancy will most likely go to term, and the labor be entirely uncomplicated. Nor need we anticipate that the paralysis will be more severe than usual because of the pregnancy. Both conditions, the pregnancy and the paralysis, will follow uninfluenced courses in the majority of cases.

It is interesting to note that there has been no instance of intra-uterine poliomyelitis. The work of immunologists has indicated that there is a transmission of absolute passive immunity from the mother to the offspring. Unfortunately, this does not persist, for a number of instances of acute anterior poliomyelitis in children under the age of one month have been reported.

#### PREGNANCY FOLLOWING PREVIOUS ACUTE ANTERIOR POLIOMYELITIS

In this part of our study, we analyzed the data relative to 243 patients who had been paralyzed by previous acute anterior poliomyelitis for 1 year or more prior to pregnancy. The analysis was conducted by dividing the cases into 3 groups. Group A included those in whom deliveries were spontaneous or effected easily, group B those in whom deliveries were effected with difficulty. There were 201 cases in groups A and B, excluding 8 patients who were pregnant at the time that the analysis was completed, 7 of whom were primipare and 1 a secundigravida who had previously miscarried. The third group, X, included 34 cases for whom the data were relatively in-

TABLE V—COMPLICATIONS IN MOTHER (209 CASES) AND OFFSPRING (361 CASES)—  
GROUPS A—B

Complications		No of cases
<b>a During pregnancy</b>		
1	Abortion	35
a	Therapeutic	8
b	Spontaneous	22
c	Self-induced	5
		20, 9 5%
2	Toxemia of Pregnancy	
a	Nausea and vomit- ing	7
b	Hypertension and al- buminuria	12
c	Nephritis	1
d	Eclampsia	2
		22, 10 53%
3	Hypertension	6
4	Cardiac disease and decompensation	3
5	Pyelitis, toxic thyroid, uterine fibroid, placenta previa, premature separa- tion of placenta, ruptured uterus, diabetes mellitus, secondary anemia	1 each
<b>b Following pregnancy (in mother)</b>		
1	Postpartum hemorrhage	4
2	Pyelitis	3
3	Phlebitis	3
4	Cardiac decompensation	3
5	Nephritis	2
6	Shock, uterine sepsis, adherent placenta, pulmonary tuberculosis and acute yellow atrophy of liver, death following eclampsia, varicose veins of leg, cystocele and rectocele, toxic goitre, renal calculus	1 each
<b>c In offspring</b>		
1	Death	
a	Prolapsed cord	2
b	Cerebral hemorrhage	2
c	Monster	1
d	Pneumonia	1
e	Cause unknown	16
		22, 5 4%
2	Convulsions, anemia of newborn, hydrocele, bilateral undescended testicle, facial paralysis (instru- mental), bilateral club-foot, uni- lateral club-foot	1 each
Group A—cases delivered with ease		
Group B—cases delivered with difficulty		

adequate. The incidence of paralysis, the incidence of deformity and the frequency of employment of orthopedic reconstructive procedures were all greater in group B in which there was greater difficulty in labor than in group A (Table III). In 28 cases in whom the pelvis was studied both roentgenographically and by external pelvimetry, we were impressed by a fact that has been stressed by many workers, namely, that the external and internal pelvic measurements alone are less accurate than roentgenographic pelvic measurements in determining the pelvic adequacy for parturition. In these 28 cases, roent-

TABLE VI.—DATA RELATIVE TO GESTATION

Duration of labor in 364 deliveries (groups A and B) ( <i>non</i> paralytic females)		Type of presentation in 364 deliveries (groups A-B) ( <i>non</i> paralytic females)		Incidence percentage in 364 deliveries as to forceps breech (Standard)
No. of hours	No. of cases	Presentation	No. of cases	
No. less of labor	27	Vertex	304	84.4
Less than 1 hour		Breech	18	5.1
1 to 5 hours	40	Transverse		6.6
6 to 10 hours	23			
11 to 15 hours	6	Face		1.7
16 to 20 hours	2			
21 to 25 hours		Unknowable		
26 to 30 hours				
31 to 35 hours				
36 to 40 hours				
41 to 45 hours				
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966 to 970 hours				
971 to 975 hours				
976 to 980 hours				
981 to 985 hours				
986 to 990 hours				
991 to 995 hours				
996 to 1000 hours				

favorably with the averages given by Jarcho for 200 normal females.

The number of pregnancies in the entire series varied from a minimum of 1 to a maximum of 10 and the number of deliveries from a minimum of 1 to a maximum of 9. Fifty per cent of the patients were pregnant at least once the remainder delivering two or more times. In 209 cases there were 410 pregnancies, while in 201 cases there were 361 deliveries, excluding 35 abortions (Table IV). Fourteen patients were still pregnant at the time that this analysis was completed. Complications such as abortions, 9.56 per cent, toxemia of pregnancy, 10.53 per cent, and postpartum hemorrhage, pyelitis, phlebitis, nephritis, uterine sepsis, cardiac decompensation and adherent placenta occurred in percentages almost identical to the statistical reports of such complications in *non paralytic females* (Table V).

The duration of labor varied from 1 to 76 hours. The average number of hours of labor in the primiparous women was 10.05 hours, and in the multiparous patients was 9.06 hours (Table VI). Of 361 deliveries in groups A and B, 84.76 per cent were vertex, 3.32 per cent were breech, 0.55 per cent were transverse, 0.37 per cent were face while data were inadequate in 11.1 per cent. Sixty-five per cent were delivered normally or spontaneously with or without an anesthetic, 21.0 per cent by forceps, 11.54 per cent by cesarean section and the 4 remaining cases by breech extraction and internal podalic version. It is difficult to compare the incidence of the utilization of forceps in non-paralytic females and paralytic females, because of the tendency in different clinics to utilize elective forceps in a variable percentage of cases. Forty-seven cesarean sections were performed in our series of 407 deliveries, an incidence of 11.54 per cent, which is very high as compared to the frequency of utilization of this procedure in non-paralytic cases. We believe however that there are many factors which have served to create this high percentage and that this figure does not indicate this procedure to be more frequently necessary in effecting delivery in paralytic females. For example there were 11 cases in which cesarean section was definite

## TYPE OF DELIVERY

In 407 deliveries (215 cases in groups A, B and C)

Type of delivery	No. of deliveries	Incidence % in 407 deliveries	Percentage incidence of cesarean section in non-paralytic females
Normal (spontaneous with or without anesthesia)	264	64.86	
Forceps	83	20.39	91 (Williams), 89 (Nelson), 74 (Minkler)
Cesarean section	47	11.54	11.1-12.5 (Williams quoted by Minkler)
Breech extraction		0.00	
Internal podalic version		0.00	
Unknowable data	7	1.74	

Group A—cases delivered with ease.  
Group B—cases delivered with difficulty.  
Excluding 5 cases who were pregnant at time when analysis was completed, of whom were 209 pregnancies and 361 deliveries who had previously miscarried.

geographed by the Thoms grid method there was oblique contraction of the pelvic inlet in 75 per cent while in 25 per cent the inlet was symmetrical. The average measurements of the pelvis in these cases compared

TABLE VII—INDICATION FOR CESAREAN SECTION

		No. of cases having cesarean sections	Indications for cesarean section in non-paralytic females (percentage incidence)	
Total—47 cesarean sections in		38	(Williams quoted by Stander)	444 cesarean sections
a Definite Indications Dystocia	1 Causes possibly related to poliomyelitis—Contracted and deformed pelvis Abdominal weakness in only 1 case	4	Contracted pelvis 72.80 Toxemia of pregnancy 7.45 Other factors 19.75	Disproportion 37.4 Eclampsia } Toxemia of pregnancy } 27.0 Other factors 17.4
	Test of labor		Premature separation of placenta	Tumors Phlebitis Heart disease Myelitis Incomplete rupture uterus Elderly primipara etc.
	2 Causes not related to poliomyelitis—Large fetal head, premature separation of placenta, obstruction by non gravid horn of bicornuate uterus, cardiac decompensation, rigid cervix, uterine inertia, transverse arrest, midpelvic impaction, etc.	7	Placenta previa Tumors Heart disease Elderly primipara, etc.	For sterilization 3.7 Because of previous cesarean section 18.7 Placenta previa 8.3 Premature separation of placenta 1.3
b Questionable Indications  No Test of Labor	1 "Small pelvic measurements" according to obstetrician. No x ray study and measurements No other pregnancies	16		
	2 For sterilization purposes	3		
	3 No reason given. Other pregnancies in these cases were normal (spontaneous) or by forceps	4		
	4 Toxemia of pregnancy	1		
	5 Other reasons—example obstetrician felt better' etc.	3		

ly required, but of these only 4 had indications possibly related to the poliomyelitis. These 4 patients had contracted and deformed pelvis with a disproportion between the fetal head and the maternal pelvis and a failure of progression after a test of labor. The indications in the 7 other cases were definitely non-poliomyelitic factors (Table VII, a). In the 27 remaining cases, the indications were less definite. In some instances the obstetrician was guided by clinical pelvic measurements as indicative of cephalopelvic disproportion without the benefit of a roentgenographic study. In others the indication was surgical sterilization, even though in many instances previous pregnancies had been effected normally or by forceps (Table VII, b). It becomes difficult, therefore, to evaluate this factor except to conclude that the figure of 11.54, representing the incidence percentage of cesarean section in our analysis, is probably an exaggerated estimate of the exact indication of this procedure in paralytic females.

Three hundred and sixty-one children were delivered to 201 paralytic females in groups A and B. The complications that occurred in the children during or shortly after birth were no different and no more frequent than those in children born of non-paralytic females (Table V, c). There were bilateral clubfoot

and unilateral clubfoot deformities in 1 case each, but there was no other evidence of paralysis in these children. Facial paralysis in 1 instance was probably due to a difficult forceps delivery. There was no evidence of intra-uterine transmission of poliomyelitis to the offspring in any of our cases.

Of special interest to us, as orthopedic surgeons, is the fact that none of the reconstructive orthopedic procedures employed to rehabilitate these patients exerted any adverse effect on the course of delivery. There were spine fusions performed in 6 patients, and even though in some instances this included the lumbosacral area, the course of labor was not affected. In 1 patient with a surgically fused hip and a secondary 15 degree adduction deformity, there was a spontaneous delivery with the patient in the Sims position. There was no instance in which the patient had had a previous abdominal fascial transplant. Dr. Charles Leroy Lowman has written us that in his 1 patient who had become pregnant subsequent to an abdominal fascial transplant, no difficulty was encountered, and that at the present time the transplants are apparently working satisfactorily.

It becomes apparent, therefore, that not only in acute cases but also in the patients paralyzed for long periods, a normal course of

gestation and labor may be anticipated in the absence of complications. The incidence and type of complications of pregnancy are practically the same in paralytic and non-paralytic females, except perhaps in the use of cesarean section. We believe that the high incidence of cesarean section found in our study was due to the improper selection of the procedure in many of the instances. The termination of the delivery in paralytic women may have to be assisted by some maneuver such as manual extraction or forceps. This can hardly be called a complication since it is frequently employed in the final stage of labor for nonparalytic women and causes no appreciable damage to maternal or fetal tissues. There has been no evidence of intra-uterine transmission of poliomyelitis from the mother to the offspring in our series.

#### CONCLUSIONS

Our study of the obstetric experiences of paralyzed women leads us to the following conclusions.

1. Asymmetry of the pelvic inlet is found in approximately 80 per cent of the pelvis of women who have had infantile paralysis. The distortion is mild in the majority of cases so that it does not produce dystocia. Asymmetry of the pelvis is absent in those who because of extensive paralysis are either completely bedridden never having attempted to bear weight on either lower limb or get about with braces and crutches, bearing most of the weight on the arms. The pelvic asymmetry is undoubtedly due to a combination of factors, one of the most important of which is rotation of the pelvic ring consequent upon and secondary to a lumbosacral rotary-lateral scoliosis. Weight bearing is also instrumental in the causation of deformity of the pelvic ring. This factor is dependent upon (a) the degree of rehabilitation of the patient by the use of external appliances or orthopedic reconstructive procedures or both, and (b) the degree of atrophy and underdevelopment of the associated bony pelvis. Other factors, such as shortening of a lower limb and muscle imbalance are instrumental especially where they initiate or exaggerate a lumbosacral scoliosis.

Attention has been called to 4 types of deformity of the pelvis as a whole (1) lateral pelvic obliquity (2) increased anterior pelvic tilt with exaggerated lumbar lordosis (3) anteroposterior axis deviation or rotation about a longitudinal axis, and (4) rotation of one innominate bone upon the other in nominate bone about a transverse axis or torsional deformity.

2. From an analysis of 25 cases reported in the literature 1 case communicated to us, and 13 cases collected by ourselves, we conclude that pregnancy complicated by acute anterior poliomyelitis may be anticipated to progress normally with a normal termination of labor and with a normal offspring. The involuntary contractions of the uterus and the ability of the uterus to expel its contents spontaneously observed also in patients paralyzed by cord tumors, spondylitis, and vertebral fracture are due to the fact known to physiologists, that the uterus has an independent nerve supply and will contract not only after the spinal cord is transected but even after its sympathetic nerve supply is extirpated. There was no instance of intra uterine poliomyelitis in these 29 cases. The passive immunity of the offspring derived from the mother does not persist for long since a number of cases of acute anterior poliomyelitis under the age of 1 month (earliest, 9 days) have been reported.

3. An analysis of 243 patients, who became pregnant one year or more subsequent to an acute attack of anterior poliomyelitis indicates that a normal and uneventful pregnancy and labor with a normal offspring may be anticipated in these cases. There is no indication for interruption of the pregnancy at any stage except for those reasons that would be operative also in non-paralytic females. The complications prior to and following delivery in paralytic females are on the percentage basis, almost identical with those in non-paralytic females. Although it is true that in our analysis of paralytic females, cesarean section was utilized in a higher percentage of cases than in a comparable series of non paralytic females, it is our belief that the indications for this procedure in some instances may not have been warranted, and that, therefore this percentage probably does

not represent the true index of the need of this procedure in paralytic females

## REFERENCES

- 1 BRAHDY, M B, and LENARSKY, M Acute epidemic poliomyelitis complicating pregnancy J Am M Ass, 1933, 101 195-198
- 2 CALDWELL, W E, and MOLOY, H C Anatomical variations in the female their classification and obstetrical significance Proc Roy Soc Med, 1938, 32 1-30
- 3 CALDWELL, W E, MOLOY, H C, and D'ESOP, D A Further studies on the pelvic architecture Am J Obst. & Gynec, 1934, 28 482-497
4. HORNING, R, and CREUTZFELDT, H G Laehmungen vom Landry'schen Typ in der Schwangerschaft Deutsche med Wchnschr, 1930, 56 1470-1477
- 5 JARCHO, J The Pelvis in Obstetrics A Practical Manual of Pelvimetry and Cephalometry Including Chapters on Roentgenological Measurement New York Paul B Hoeber, Inc, 1933
- 6 McGOOGAN, L S Acute anterior poliomyelitis complicating pregnancy Am J Obst & Gynec, 1932, 24 215-223
- 7 MILLER, J R Cesarean section at the Hartford Hospital, 1904-1927 New England J Med, 1928, 199 651-656
- 8 MILLER, N F Anterior poliomyelitis complicating pregnancy, with report of 2 cases J Michigan State M Soc, 1924, 23 58-61
- 9 MORROW, J R, and LURIA, S A Pregnancy complicated by acute anterior poliomyelitis J Am M Ass, 1939, 113 1561-1563
- 10 MOSHER, G C Cesarean section, indications and limitations Surg, Gynec. & Obst, 1927, 45 655-665
- 11 RENAULT, J, and MARTINGAY, M Poliomyélite aigue avec pôleoencéphalite chez une femme enceinte Guérison complète Accouchement normal d'un enfant normal Bull. et mém Soc. méd d hôp de Par, 1911, 31 344-350
- 12 RUHL, H Ueber Poliomyelitis und Graviditæt Zentralbl f Gynaek, 1939, 22 1268-1271
- 13 SCHELL, J T Myelitis complicating pregnancy New York M J, 1906, 83 657-658
- 14 STANDER, H J Williams' Obstetrics A Textbook for the Use of Students and Practitioners 7th ed New York and London D Appleton & Co, 1936
- 15 THOMS, H The Obstetric Pelvis Baltimore Williams & Wilkins Co, 1935
- 16 WILLIAMS, J W A critical analysis of 21 years' experience with cesarean section Bull. Johns Hopkins Hosp, 1921, 32 173-184
- 17 ZIMMERMAN Ueber die Ursache schneller Spontangeburt bei Erkrankungen des Rueckenmarks Zentralbl f Gynaek, 1914, 38 849-852

## LIVER CELL FAT NECROSIS CAUSED BY PANCREATIC REFLUX

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**D**URING the past 20 years, in addition to the investigation of specific changes in the liver itself research has been made along two lines concerning the relationship of the liver to other organs. Functionally in so far as the metabolism of hemoglobin and its derivatives, the bile pigments, is concerned, the liver is closely related to the spleen. Surgically the close topographical relation of the liver and the pancreas is very important, especially when disease of the gall bladder and pancreas is being treated. However the pathological problems arising within the hepatopancreatic system are due not only to their close proximity their close connection of blood and lymph supply but also to the proximity of the two excretory ducts in the papilla of Vater. The mechanism which transforms the two outlets, that of the liver and that of the pancreas, into one communicating system of channels lies in the occlusion of the common outlet for both in the papilla of Vater. The diverticulum thus becomes transformed into a sort of pot in which the two secretions are mixed. The difference between hepatic and pancreatic secretory pressures determines into which duct the mixture is forced. The relatively high incidence of anatomical variations in the mutual position of the ducts and their openings reduces the probability of the reflux for instance, when the pancreatic duct opens outside of the diverticulum, the occlusion of the papilla has no influence on the pancreas. Three main types of occlusion may occur as the result of stones, spasm or edema of the duodenal mucous membranes. The most important cause is stones. Since Opie and Halsted published their classical papers, numerous other cases have been observed and

reported by various authors (Truhart, Korte, Schottmüller, Schmieden and Schering and particularly Cameron and Noble). In some of these cases congestion, the result of retention of pancreatic secretion with its subsequent hemorrhagic pancreatic necrosis, was the only observation made.

It has been safely established that occlusion of the papilla by any mechanism may cause passive congestion in the pancreatic ducts by back pressure of the pancreatic juice and that this congestion may be followed by rupture and bursting of the duct walls and umbilication by the pancreatic tissue of the coagulating pancreatic secretion. In this manner is produced the well known pathology of pancreatic necrosis and later intraperitoneal fat necrosis. This process has been thoroughly investigated particularly by Opie, Balo and Ballon, Westphal, Archibald and many others. The importance of retention of pancreatic secretion as an etiological factor in acute pancreatic necrosis is well established, in spite of the fact that, as is well known to pathologists, at autopsy in cases of acute pancreatic necrosis the hemorrhagic destruction of the gland makes it generally impossible to find the spot where the rupture of the duct occurred. It is much more difficult, however to give accurate proof or evidence of the reflux. Here we must distinguish between two possibilities: first, bile flowing in the pancreatic ducts, and second pancreatic secretion flowing in the bile duct.

From clinical and pathological observation, there is better and more convincing evidence for a reflux from the liver to the pancreas. Colp and his collaborators made this reflux visible by x ray in patients with gall bladder drains, after the injection of morphine to produce a spasm of the sphincter of the papilla. They explain certain cases of acute pancreatitis by this mechanism, as does Opie, Halsted and H. L. Popper.

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The pathological changes which are produced by the presence of pancreatic secretion in the bile ducts and in the gall bladder have been investigated, experimentally, by a great number of authors. Conclusive evidence emerges from the biochemical examination of bile collected directly from the bile ducts or gall bladder during operation. The presence of pancreatic juice can be checked by qualitative tests for three pancreatic ferments: amylase, trypsin, and lipase. Most investigators have utilized amylase determinations for detecting the presence of pancreatic secretion because of the relative simplicity with which these determinations can be made, technically speaking. The most common method used is the so called dilution method of incubating equal quantities of carbohydrate solutions with increasing dilutions of amylase (diastase) containing fluid and determining the highest dilution at which digestion still occurs. Such ferment titrations have been carried out by Nordmann, Bundschuh, Ruppner, Driembowski, Brackertz, Colp, Werthemann, and Westphal. The most extensive examination was carried out by H. L. Popper, who examined 219 specimens of bile gathered during surgical operations and found that 37 specimens or 17 per cent of all the cases gave evidence of pancreatic reflux by the amylase dilution method. Since bile normally contains a small amount of amylase as Hofman noted for the first time in 1845, only high concentrations prove the presence of pancreatic secretion. This concentration must exceed that increased concentration of amylase in bile which occurs during carbohydrate feeding, as discovered by Bonnano in 1908. It is only when the highest, still active dilution of bile exceeds the highest, active dilution of serum, which also physiologically contains small quantities of amylase, that the case can be diagnosed as one of pancreatic reflux. H. L. Popper fixes this limitation at  $d\ 38/30 = 64$ . Of Popper's 219 cases, 19 were cases of acute or chronic pancreatitis. Among the 200 remaining cases without pancreatic disease, 20 cases, or 10 per cent, showed the presence of pancreatic ferment in the bile. This means that approximately every tenth case of surgical bile-duct or gall-bladder disease is com-

plicated by pancreatic reflux. In view of the fact that this reflux is anatomically possible in only a limited percentage of individuals, Popper's high figure of the actual incidence of pancreatic reflux proves that this reflux is a rather common complication.

Much less work has been done for the determination of the pancreatic ferment, trypsin, in bile. Technically, the determination is much more difficult than that for amylase and the evidence given by a positive test is not nearly as convincing as that for amylase, for bile frequently gives a positive trypsin reaction especially when it contains a large amount of protein. Another serious drawback is the relatively low specificity of positive findings for trypsin administered into the bloodstream may be excreted by the liver in the bile, or trypsin may develop from leucocytes in cases of cholecystitis, or lastly, it may come from the duodenum as a result of regurgitation of duodenal contents through the patent papilla. Consequently, only a few trypsin determinations of bile have been reported by H. L. Popper, Hoesch, Westphal, and Loeffler. Erb and Barth examined 50 specimens of bile from cases of cholecystectomy and found that 38 per cent, using the Mueller-Jochmann method, and 74 per cent, using the Fuld-Gross method, were positive for trypsin. These investigators admit that the high positive incidence may have been caused partially by the presence of leucocytes.

A few determinations of lipase in pathological bile have been made. Although lipase does not deteriorate as rapidly as trypsin, as Colp and Doubilet have pointed out, and although it is much more specific than trypsin, for normal bile contains no lipase or only traces thereof (Bonnano, Sobotka) lipase determinations are complicated. H. L. Popper, using the stalagmometric method of Rona and Michaels, found no increase in the lipase contents of bile in a case of chronic cholelithiasis with fat necrosis of the omentum and with a normal pancreas but did find a slight increase of lipase in the bile of a patient with a normal gall bladder, normal bile ducts, and a normal pancreas, who had cramps for 6 years following a laparotomy which revealed edema and hemorrhagic exudate of the pancreas.



Evidence of the presence of pancreatic ferments in the gall bladder proving reflux of pancreatic secretion is of practical and clinical interest only inasmuch as this condition may produce a nonperforative form of biliary peritonitis. It leaves unanswered the question to what extent is the liver or better still, are the liver cells, involved by the reflux. The bile ducts particularly the common duct, are immune against pancreatic secretion. Numerous observations have been recorded concerning liver pathology in cases of pancreatitis and particularly in cases of pancreatic necrosis. In most of these reports, the liver pathology is co-ordinate with the pancreas pathology.

Adamaki described multiple thromboses of the portal vein capillaries with military hepatic necrosis in a case of pancreatic necrosis complicated by suppurative cholecystitis and cholelithiasis.

Oesterreich investigated a case of initial cirrhosis and moderate jaundice with chronic (scarry) fibrosis of the pancreas. In the mesentery and the omentum numerous foci of fat necrosis were present, but the pancreas itself appeared to be free. The omentum was adherent to the capsule of the liver and, in the field of these adhesions, the liver showed numerous subcapsular triangular areas of necrosis. Oesterreich explains that this necrosis is the result of pancreatic ferments carried to the liver from the pancreas through the adherent omentum, from which numerous small vessels entered the liver surface.

Rodolf published the report of a case of septic endocarditis with multiple small focal necrotic areas in the pancreas and with severe passive congestion and fatty degeneration of the liver. The latter showed small rather nonspecific foci of necrobiosis which Oesterreich describes and explains as septic, mentioning only as a hypothesis the possibility that pancreatic ferments might have reached the liver parenchyma by way of the portal vein. The same hypothesis was raised by Wiesel who found marked focal fatty infiltration with a nonspecific necrosis in the liver in 4 cases of pancreatic necrosis. It is worth mentioning that he saw fat cell emboli in these cases which he traced back to the pan-

creas in the interlobular branches of the portal vein.

Miller likewise in his case saw fat cells in the intrahepatic ramifications of the portal vein.

Synak and Nakamura found fat cirrhosis of the liver with old blood pigment associated with pancreatic necrosis. H. Mary found marked and partially focal areas of fatty degeneration of the liver. Rankenberg noted focal passive congestion due to thrombosis of the branches of the portal vein. Eloesser found parenchymatous and fatty degeneration of the liver combined with hemorrhagic pancreatitis.

Truhart in his book on pathology of the pancreas diseases, reported 47 cases of pancreatic fat necrosis with jaundice. Among these 12 had either cholelithiasis or obstructing tumors of the bile ducts. In the 35 remaining cases the cause of the jaundice could not be explained. The liver in these patients showed fatty and parenchymatous changes of a nonspecific nature.

Marx observed 2 cases of severe parenchymatous hepatitis with marked focal fatty infiltration and degeneration and pancreatic fat necrosis. He explained the pathology of the liver foci as caused by toxins or toxic products of metabolism carried to the liver by the portal vein.

Eloesser examined cases of his own and reviewed the literature concerning liver pathology associated with pancreatic necrosis. He described the typical liver as one revealing pale yellow more or less sharply circumscribed areas alternating with dark red soft, depressed islands on cut surface and microscopically revealing fatty degenerations and congestion resulting eventually in focal necrosis. He points out that such hepatic changes are found frequently in case of severe passive congestion or cirrhosis without pancreatic necrosis. Berner who investigated the organs of 5 cases of pancreatic fat necrosis 2 of them with alcoholic cirrhosis, describes marked fatty degeneration involving particularly the periphery of the liver acini. The interpretation of his microscopical analysis seems to be doubtful since the crescents he described in the sudan stained section are artefacts so

frequently found when this stain is used. However, he did find in some of his cases single fatty acid crystals in the liver which gave a positive green Benda reaction. It is quite likely that some of his cases did contain foci of intrahepatic fat necrosis but that he was unable to demonstrate this because of imperfect histological technique. His paper, which dates back to 1907 when the histological presentation of fat and fat necrosis was not as yet well developed, is the only reference found, which in the descriptions and illustrations gives a clue of specific intrahepatic fat necrosis. However, Berner in the discussion of the findings does not mention this possibility. In a large series of experiments Fischler has noted severe degeneration of the liver in dogs after having established an Eck's fistula and provoked a pancreatic fat necrosis. He found severe centro-acinar degeneration, atrophy, and necrosis, but he emphasizes that he never saw salts of fatty acids, soap or pure fatty acids, which indicate specific fat necrosis. Since in his experiments the portal blood stream to the liver was blocked, he had to trace back the liver pathology to toxic products reaching the liver by way of the lymphatics. This is possible with dogs, for this animal possesses a network of interacinar lymph vessels especially around the central vein as described by H. Popper. Hildebrandt has questioned the experiments of Fischler and tried to prove that the degenerative liver changes are caused neither by the Eck's fistula nor by pancreatic fat necrosis but by the chloroform used for narcosis.

When studying the possibility of proving, by microscopic evidence of liver pathology, the presence of pancreatic reflux into the liver, we must consider the action of the three pancreatic ferments. The action of amylase cannot be demonstrated histologically. The action of trypsin could be proved by necrosis. However, focal necrosis of the liver is very common in such conditions as passive congestion, cirrhosis, parenchymatous hepatitis, etc. when it becomes more severe and tends to lead to yellow or red atrophy. It would be difficult to differentiate focal interacinar necrosis of this nonspecific type from specific necrosis caused by the presence of trypsin.

Also it is very doubtful whether pancreatic trypsin coming in contact with liver parenchyma would digest or damage it. In order to develop its specific action, trypsin must first be activated. In the duodenum enterokinase acts as the activator of the trypsin. Bile contains no activator of trypsin as has been pointed out by Oppenheimer. For this reason several authors, Hoesch, Frank, Moynihan and others, believe that simple bile reflux in the pancreatic duct is not sufficient to cause acute pancreatitis. They feel that only if the bile is contaminated by bacteria as a result of a cholecystitis or passage of bacteria from the duodenum through the papilla of Vater will pancreatic trypsin become activated and cause pancreatic necrosis. The causative rôle of cholecystitis in pancreatic diseases has been discussed by E. Starr Judd.

Whereas trypsin needs specific activators, the third ferment of the pancreas, lipase, is much more easily activated. Pure bile can act as an activator and bile salts enhance the fat splitting action of lipase (Fuerth and Schuetz, Terroine, Mellanby and Woolley, Sobotka). Even normal tissues may activate pancreatic lipase as is proved by the fact that numerous cases of intraperitoneal fat necrosis have occurred in which there has been no evidence of mixture of bile with pancreatic juice. This knowledge has been gained from autopsies and has been confirmed experimentally by Frugoni and Stradiotti who produced typical peritoneal fat necrosis in animals by intraperitoneal injection of fresh sterile pancreatic juice, thus proving that neither bile nor bacteria are necessary for the activation of pancreatic lipase. It must be mentioned that Kestner carried out analogous intraperitoneal injections in cats and dogs without producing fat necrosis. However, it appears that there was some technical error in his experiments, for he succeeded in producing fat necrosis in only 50 per cent of his cases when he used equal parts of bile and pancreatic juice. The rôle of bile as an activator of pancreatic enzymes was demonstrated in very convincing experiments by Rewbridge who produced a free flow of bile into the peritoneal cavity in dogs by perforating and opening the gall

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Fig. 1. Small focus of fat necrosis in large artery.  $\times 30$ .



Fig. 2. Large area of fat necrosis at the periphery of an artery.  $\times 30$ .

In the frozen sections large number of fine fat needle crystals could be seen in these foci forming small masses which gave a positive green Benda reaction. Under the polariscope these were double refracting needles (Figs. 3, 4). In the paraffin sections stained with Azan or Mallory's stain, these foci revealed an amorphous yellow staining ground which duplicated, to a certain extent the acinar structure of the surrounding liver trabeculae. When stained with argentophil fibers, the network of fibers in the necrotic areas remained essentially unchanged (Fig. 5). This again supports the evidence that lipase had destroyed the fat only but not the fibrous skeleton of the tissue. Careful examination of a large number of slides revealed a few small liver acini, particularly localized within the thick periportal septa which had undergone similar but complete fat necrosis (Fig. 6).

The microscopic examination of the pancreas revealed the typical picture of an acute hemorrhagic necrosis. All over the tissue were scattered irregu-

larly shaped, large and small foci of necrosis with secondary hemorrhages. In the intralobular tissue there was a typical necrosis with a positive green Benda reaction. In the glandular tissue the necrotic areas were densely infiltrated by leucocytes, particularly in the borderline zone (Fig. 7). The medium and small excretory ducts were the seat of marked inflammatory infiltration of the muscular wall with partial destruction and partial reepithelization of the columnar epithelium and dense leucocytic infiltration of the periductal tissue. The lumen of many of the small ducts contained leucocytes which surrounded oval or spindle shaped, pale pink staining, translucent corporcles which were produced from the protein of the inflammatory process by clotting and subsequent condensation.



Fig. 4. Liver intralobular fat necrosis. Fat acid crystals of fat necrosis under the polariscope.

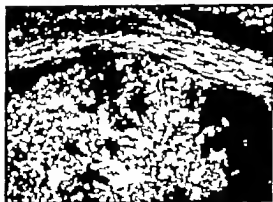


Fig. 3. Fatty acid crystals at the periphery of an area of fat necrosis in the liver. Frozen slide Benda reaction, counter staining with nuclear fast red.  $\times 70$ .

In addition to the long complemented fatty acid needles in the field of necrosis, the polariscope shows great number of small single point crystals scattered all over the tissue. Exact demonstration given evidence that these crystals lie in the fat drops of the degenerated liver as is usually at the periphery of the single drops. These crystals are not specific for the action of pancreatic lipase but develop after which all sections of fatty carbohydrates, the most kind is known. The heavy chain formed inside the nucleus of tissue both these microscopic subjects be found in the case of necrotic action of lipase.

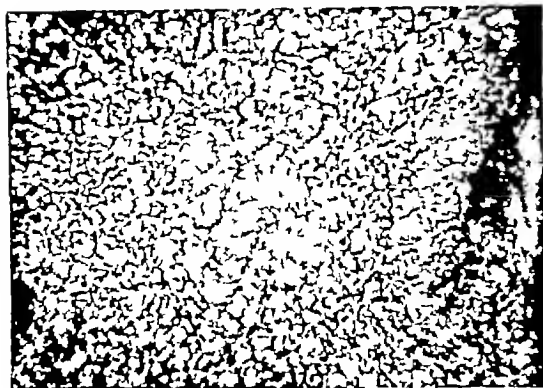


Fig 5 Intercellular network in an area of intra acinar fat necrosis  $\times 65$

It is very likely that these protein bodies, by secondary precipitation of the mineral salts, gave origin to the little stones found in the main duct (Fig 8)

Biochemical analysis of the pancreatic stones, by Dr G Weber Schimpff of the Biochemical Laboratory of the Cook County Hospital, revealed that they consisted of calcium carbonate mainly with a small amount of phosphates and some organic matter adherent to the surface (Two of these stones were soft and gray with a jagged, rough surface approximately 4 millimeters in diameter, another stone found was only 1 millimeter in diameter)

For the presentation of fat necrosis in this case and in many others, the old method of Benda published in 1900 proved very useful. Lapinan, in 1902, found that it was not necessary to use the original fluid which Weigert applied for the presentation of neuroglia but that it was sufficient to fix the tissue in forma-

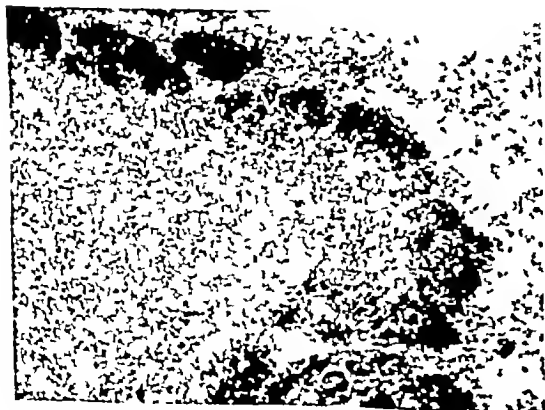


Fig 7 Focus of pancreatic necrosis with cellular debris in the center and a peripheral zone of well preserved glandular tissue  $\times 31$



Fig 6 Small pseudo acinus located in the thickened and inflamed periacinar capsule, completely destroyed by fat necrosis  $\times 30$

lin and then immerse it in a solution of copper acetate. Fischler and Gross applied concentrated aqueous copper acetate solutions for 2 to 24 hours at 37 degrees C. This is necessary for the staining of palmitic and of stearic acid but oleic acid takes on the stain almost immediately at room temperature. I had the best results by counter staining with nuclear fast red and mounting the frozen sections in a concentrated aqueous levulose solution. A very excellent presentation of fat necrosis can be accomplished by use of Goemoeri's new method (oral communication). Frozen slides are immersed in a 2 to 5 per cent aqueous solution of cobalt nitrate or cobalt chloride

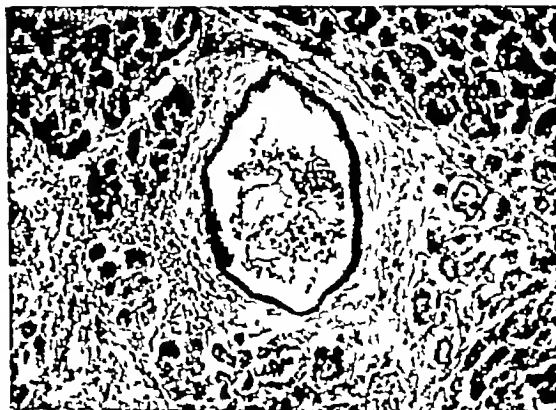


Fig 8 Pancreatic duct. Inflammatory proliferation of epithelium right side, protein bodies and leucocytes in the lumen  $\times 65$

Then they are thoroughly washed in distilled water and finally placed in a 1 per cent watery ammonium sulfide solution. The necrotic fat tissue stains dark black and all the other constituents of the tissue remain unstained. As a counterstain nuclear fast red or light green can be used.

In order to utilize the case here reported in the study of pancreatohepatic reflux, two pertinent questions must be answered: (1) Is the necrosis in the liver specific, i.e. is it produced by the lipase of the pancreas? (2) Did the pancreatic secretion provided it was the pancreatic lipase that caused the necrosis, reach the liver parenchyma by way of the bile ducts or does the possibility of transportation through lymphatics or blood vessels have to be considered?

Concerning the first question, the possibility of nonspecific fat necrosis has been emphasized.

A warning must be given to the examining pathologist not to trace back every necrosis of the subcutaneous, mesenteric or retroperitoneal fat to the pancreas but to consider trauma, impaired circulation infection, etc. as possible etiological factors. Nonspecific necrosis of fat tissue has been observed under different conditions and in various organs. Abrikosoff and Lecène and Moulouguet described fat necrosis and granulomas as a result of disturbed circulation in the subcutaneous fat tissue. Dupont and Perrot described cystic foci of necrosis in the fat of breasts of elderly women. Teutschlander described necrosis of the intracapsular fat of mesenteric lymph nodes, etc. In all these cases the character of the necrotic areas was different from that seen in specific pancreatic fat necrosis. The foci in nonspecific fat necrosis present a granular debris with only a few small accidental fat crystals and surrounding these foreign body giant cells can be seen. Obviously in these foci the splitting of the neutral fat is going on very slowly undoubtedly due to the very small quantities of ferment locally produced by the decomposing fat cells and the surrounding granulation tissue. The small quantities of soaps as well as of oleic and stearic salts which are produced are washed out immediately by the tissue fluids, whereas in specific pancreatic necrosis the following

takes place. The lipase at once splits large amounts of fat and thus produces masses of fatty acid crystals long before the surrounding tissue can produce a protective granulation tissue.

The foci of intrahepatic fat necrosis in our case are exactly like those of the pancreatic type. Even though no fat necrosis of the pancreas and the adjacent fat tissue were present, the morphology of the liver foci with the masses of fatty acid needles would point to the action of pancreatic lipase. Necrosis of liver tissue is a rather frequent pathological entity in red and yellow atrophy. However small necrotic areas are also frequently found in cirrhotic livers. Examination of a large number of slides taken from cases of liver atrophy and cirrhosis has convinced me that in these cases, as Fischler has already pointed out, the liver tissue never contains fatty acids or fat salts.

Concerning the route by which the pancreatic lipase reached the hepatic through lymph channels can be ruled out for in the human liver the lymph vessels and, as Drinker and Field and Rouvière described in the periportal field, there are no lymph spaces in the acini that would be in free communication with the small initial periportal and the larger perivascular lymph vessels. The fluid of the Disse space has to be filtered through the wall of the lymph vessels into the lumen, a process Oppinger calls permeability in one direction. The opposite process, i.e. penetration or permeation of lymph through the wall of the lymph vessels in the direction of the acinar tissue never has been observed and the possibility of such a reversed permeability never proved. In the case of dogs which have a well developed intra-acinar system of lymph channels, the transportation of pancreatic secretion to the liver through lymph vessels has been proved for example by the experiments of Fischler. Transportation of lipase by the blood stream is not likely since nowhere else in the body were foci of fat necrosis to be found.

H. L. Popper and Necheles, in a recently published paper have for the first time made accurate determinations of the enzyme content of the peripheral blood and in the thoracic

duct lymph after acute damage of the pancreas. Evidently, the concentration of lipase in the blood is too low to split fat in tissue outside of the pancreas. Even when we admit that the presence of bile produces optimal chances for activation of the lipase, this same process would occur elsewhere in the organism if large quantities of pancreatic lipase were administered by the blood stream. For the reasons stated and because of the presence of pancreatic stones of a size just large enough to block the papilla of Vater, reflux of pancreatic secretion to the liver by the way of the bile duct must be admitted.

#### SUMMARY

Pancreatic and hepatic biliary ducts may be transformed into one communicating system by obstruction of the outlet—the papilla of Vater. The most frequent cause of obstruction is stones in the common duct, however, spasm of the sphincter of Oddi and edema of the duodenal mucosa must be taken into consideration. Reflux of bile into the duct of Wirsung may cause acute hemorrhagic pancreatitis. Reflux of the pancreatic secretion into the bile ducts has been described as the etiological factor for certain liver changes of different but nonspecific character. That reflux has been proved by amylase determination of the bile. The presence of amylase is indicative in high titer only inasmuch as bile normally contains amylase in low titer, whereas, the presence of lipase in the bile is conclusive evidence of pancreatic reflux, inasmuch as normal bile contains no lipase. In this paper liver-cell fat necrosis as a consequence of lipase content in the bile is described. Lipase in the bile is conclusive evidence of pancreatic reflux, inasmuch as normal bile contains no lipase.

#### BIBLIOGRAPHY

1. ABRIKOSOFF. Ueber die spontan auftretende Fettgewebnsekrose und Fettgranulome. *Zentralbl f allg Path u path Anat*, 1906, 38, 542.
2. ADAMSKI. Lebernekrosen bei Pankreasfettgewebnsekrosen. Inaugural Dissertation, Muenchen 1921.
3. ARCHIBALD. The experimental production of pancreatitis in animals as the result of the resistance of the common duct-sphincter. *Surg., Gynec & Obst.*, 1919, 8, 50.
4. BATO and BALLOU. Effects of retention of pancreatic secretion. *Surg., Gynec & Obst.*, 1909, 48, 1.
5. BENDA. Eine makro und mikrochemische Reaction der Fettgewebnsekrose. *Arch f path Anat*, 1900, 161, 194.
6. BERNER. Histologische Untersuchungen der Organe bei Fettgewebnsekrose. *Arch f path Anat*, 1907, 187, 360.
7. CAMERON and NOBLE. Reflex of bile up the duct of Wirsung caused by an impacted biliary calculus. *J Am M Ass.*, 1924, 82, 1410.
8. COLP and DOUBILET. The clinical significance of pancreatic reflux. *Ann Surg.*, 1938, 108, 243.
9. COLP, GERBER, and DOUBILET. Acute cholecystitis associated with pancreatic reflux. *Ann Surg.*, 1936, 103, 67.
10. DRINKER and FIELD. Lymphatics, Lymph and Tissue Fluid. Baltimore: The Williams & Wilkins Co., 1933.
11. DUPONT and PERROT. Cyto-stéato-nécrose et gran-grène du sein. *An d'anat path.*, 1927, 4, 531.
12. FLOESSER. Die in den letzten 10 Jahren an der Heidelberger chir. Klinik beobachteten Facille von Pankreaserkrankungen. *Mitt a d Grenzgeb d Med u Chir.*, 1908, 18, 195.
13. FISCHLER. Ueber das Auftreten akuter schwerster Leberdegenerationen an Tieren mit Eck-scher Fistel bei komplizierender Pankreasfettnekrose, nebst Bemerkungen ueber die Beziehungen zwischen Leber und Pankreas. *Deutsche Arch f klin Med.*, 1910, 100, 329.
14. Idem. Weitere Mitteilungen zu den Beziehungen zwischen Leberdegenerationen und Pankreasfettgewebnsekrose an Tieren mit Eck-scher Fistel und ueber die Moeglichkeit ihrer Verhuetung. *Deutsche Arch f klin Med.*, 1911, 103, 156.
15. FISCHLER and GROSS. Ueber den histologischen Nachweis von Seife und Fettsaeure und die Beziehungen intravenoes eingefuehrter Seifenmengen zur Verfettung. *Beitr z path Anat u z allg Path.* 1905, suppl. vol 7, 326.
16. FRUGONI and STRADIOTTI. Experimenteller Beitrag zur Kenntnis der Fettgewebnsekrose. *Berl klin Wehnschr.*, 1910, 47, 386.
17. HALSTED. Retrojection of bile into the pancreas, a cause of acute hemorrhagic pancreatitis. *Bull Johns Hopkins Hosp.*, 1901, 12, 179.
18. HILDEBRANDT. Zur Frage der zentralen Laeppchennekrosen der Leber und deren etwaigen Beziehungen zur Pankreasfettgewebnsekrose. *Mitt a d Grenzgeb d Med u Chir.*, 1912, 24, 652.
19. HOESCH. Ueber den primaeeren Trypsinangriff im Pankreas, in den Gallenwegen und der Leber. *Ztschr f klin Med.*, 1929, 110, 735.
20. JOHN EDWARD STARR. Relation of the liver and the pancreas to infection of the gall bladder. *J Am M Ass.*, 1921, 77, 197.
21. KESTNER. Experimentelles zur Fettgewebnsekrose. *Arch f path Anat*, 1923, 246, 305.
22. LECENT and MOULONGUET. Cyto-stéatonécrose ou saponification intracellulaire du tissu cellulaire du plexus sous-cutané. *An d'anat path.*, 1925, 2, 103.
23. LIPPMAN. Ueber die Benda'sche Reaction auf Fettnekrosen. *Arch f path Anat*, 1900, 160, 532.
24. MARX. Ueber Fettgewebnsekrose und Degeneration der Leber bei Pankreatitis haemorrhagica. *Arch f path Anat*, 1901, 165, 290.
25. MILLER. Inaugural Dissertation, Muerzburg, 1908.
26. NORMANN. Experimente und klinische Betrachtungen ueber die Zusammenhaenge zwischen acuter Pankreatitis und Erkrankungen der Gallenblase. *Arch f klin Chir.*, 1913, 102, 10.



- 27 OESTERLEICH. Fettgewebsnekrose am Pankreas mit gleichartigem Lebernekrosen. Zentralbl. f. allg. Path. u. path. Anat. 908, 9: 245.
- 28 OWE. The relation of cholelithiasis to disease of the pancreas and to fat necrosis. Bull. Johns Hopkins Hosp. 90, 19.
- 29 POWERS, H. L. Pankreassaft in den Gallenwegen. Seine pathogenetische Bedeutung fuer die Entstehung der akuten Pankreaserkrankungen. Arch. f. klin. Chir., 933, 75 660.
- 30 Idem. Pankreasfermente in der Galle. Zentralbl. f. Chir. 930, 56 55.
- 31 Idem. Zum Mechanismus des Auftretens von Pankreasfermenten in der Galle. Zentralbl. f. Chir. 930, 57 59.
- 32 Idem. Beitr. z. klin. Chir. (Braun.) 936, 64 5.
- 33 Idem. Diastasebefunde in der Galle. Med. Klin. 939, 5 218.
- 34 Idem. Untersuchungen ueber das Vorhanden sein von Pankreasfermenten in der Galle. Wien. klin. Wochenschr., 939, 42 248.
- 35 POWERS, H. L., and SELINGER. Zum Nachweis von Pankreasfermenten in der Galle. Einwirkung auf Leber Gallenwege und Pankreas. Ztschr. f. klin. Med., 930, 5 389.
- 36 POWERS, H. L. and NICKELER. Path. ys of enzymes into the blood in acute damage of the pancreas. Proc. Soc. Exper. Biol. & Med., 940, 43 230.
- 37 R. UTENHED. Zur Klinik und Pathologie der tumorartigen Pankreasnekrose. Mitt. u. d. Grenzgeb. d. Med. u. Chir., 905, 4 95.
- 38 REINHARDT. Fat necrosis in bile peritonitis. Arch. Path. 93 70.
- 39 RUDOLPH. Ueber Lebenderkennungen bei akuten Pankreasnekrosen. Arch. f. klin. Med. 906, 87.
- 40 SCHOTTENKILLER. Ueber peripankreatische Fettgewebsnekrose bei akuten Gallenstauungslebernekrosen im Duodenalstenose. Deutsche med. Wochenschr. 93 40 2.
- 41 SOMMER. Physiological Chemistry of Bile. Baltimore: Williams & Wilkins, 937.
- 42 TETWART. Pankreas pathologie. Vol. p. 28. Wiesbaden. Bergmann 903.
- 43 WERTHEIMSKO. Ueber diastatische Fermente in der Gallenblasenmucosa und deren Beziehung zur peritonitischen galligen Peritonitis und zur post mortalen galligen Inhibition. Verhandl. d. deutsch. path. Gesellsch., 91, 26 313.
- 44 WERTHEIMSKO. Die durch Dyskinese der Verdauungsorgans bedingten Pankreasfermenterkrankungen an den Gallenwegen und der Leber. Ztschr. f. klin. Med. 939, 99 15.
- 45 WHEEL. Ueber Leberveränderungen bei multipler abdominaler Fettgewebsnekrose und Pankreatitis haemorrhagica. Mitt. u. d. Grenzgeb. d. Med. Chir. 905, 14 487.

# RECONSTRUCTION OF THE PENILE URETHRA FOLLOWING TRAUMA

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IT is rare for an injury to tear out a large segment of the penile urethra without amputating or destroying the penis.

An enormous number of techniques are available for forming a new penile urethra, based largely on experience with congenital defects, chiefly hypospadias. Godard reviewed all the methods of replacing defects of the urethra. He classified urethroplastic procedures according to the portion of the urethra involved, fixed or mobile and the source and type of graft employed—stretching of urethra, grafts from prepuce, penis, scrotum, abdomen, thigh, bladder, appendix, saphenous vein, fascia lata, dog's aorta. He found that consistently good results with any one method were exceptional. He evaluated the procedures and considered pedicled grafts from the skin of the penis and the prepuce the best for mobile portions of the urethra and scrotal grafts best for the fixed urethra.

In injuries of the male genitalia, stripping of the skin of penis and scrotum is likely to occur before the urethra can be involved (Cottle's case). If the injury is severe enough to damage the urethra, the best repair materials—penile and scrotal skin, will also be damaged. Reconstructing a penile urethra after an injury, therefore, presents a different problem than does a hypospadias.

Mallard reported a plastic repair to replace  $2\frac{1}{2}$  inches of penile urethra, following gangrene due to introduction of a destructive chemical solution into the anterior urethra. Penile skin and one corpus cavernosum penis were destroyed also. He reviewed briefly the literature to date (1930) and found that most of the work was reported by European authors and that little plastic repair of this nature had been recorded in America. Mallard drew no distinction between urethroplastic procedures for congenital defects and those following trauma. After a pedicled tube graft from the thigh had failed to take, he attained a successful result with use of part of the scrotum and a pedicled tube formed from abdominal skin.

Von Rihmer reported a partial necrosis of the penile urethra following an injury which stripped the penis of its entire cutaneous covering and perforated the urethra 5 to 6 centimeters from the

external urinary meatus. After clean granulations appeared, suture of the urethral fragments about a catheter closed the defect in the urethral wall. A plastic procedure with the use of scrotal skin to form a new penile covering gave a satisfactory anatomical and physiological result.

U. Heynen reviewed the plastic replacement of urethral defects and gave special attention to perineal hypospadias. He was concerned with congenital defects.

The commonest site of injury to the male urethra is the membranous and bulbous portion. Blows on the perineum cause rupture of the urethra in this region, with or without fractures of the pelvis. The literature on this subject is extensive (Garlock).

Since Mallard's article, there have been few reports of injuries requiring plastic repair of the penile urethra.

## ANATOMY AND PHYSIOLOGY

The cavernous urethra is an epithelium lined canal extending from the superficial layer of the urogenital diaphragm to the external urethral orifice. It first enters the bulb of the penis, which lies in the superficial perineal space, passing almost directly forward. It then enters the body of the penis, following the direction of that organ—pendulous in the flaccid state, directed forward in the erect state. The bulbous portion of the urethra is therefore fixed in position, as are the prostatic and membranous portions. The penile urethra is mobile. The cavernous urethra is about 16 centimeters ( $6\frac{1}{2}$  inches) long, 6.5 centimeters (about  $2\frac{1}{2}$  inches) of this being fixed portion. The average diameter of the urethra is 5 to 7 millimeters, and is narrowest at the external urethral orifice and in the membranous urethra.

The two bulbo-urethral glands (Cowper's) empty into the beginning of the cavernous urethra. Small pockets of mucous cells in the walls of the cavernous urethra are called the urethral glands (of Littré). Nonglandular pits, called urethral lacunæ, also occur. The epithelial lining of the urethra is endodermal in origin, as it arises from a portion of the urogenital sinus.

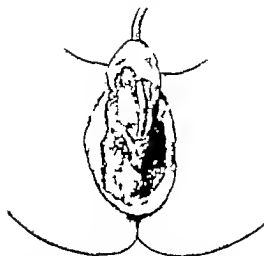


Fig. 17. Showing partial destruction of penis, loss of left testicle, scrotum, and 1½ inches of penile urethra. A rubber bridge bridges the urethral gap.

The lining of the cavernous urethra is simple or stratified columnar epithelium, with the outer cells becoming squamous in the dilatation of the urethra at its distal end—the *fovea nictitans*. The submucosa blends with the corpus cavernosum urethra—corpus spongiosum—which consists of highly vascular erectile tissue containing bundles of smooth muscle fibers.

The urethra receives its blood supply from the deep arteries of the penis, which run longitudinally in the corpus cavernosum and give off lateral branches freely. Venous drainage is into the internal pudendal veins.

The urethra serves for the passage of urine and seminal fluid. It must be patent to allow free passage of these fluid and extensible to avoid interference with erection.

#### ETIOLOGY

Inflammations, malformations and trauma may produce defects of the penile urethra.

Structure following a gonorrheal inflammation may be so severe that voiding becomes impossible. The site of those structures that require surgical intervention is the bulbomembranous segment. Strictures in the pendulous urethra are relieved by dilatation or transurethral incision. In a thousand consecutive cases treated for gonorrhea, Goldstein had 3 cases of urethral stricture necessitating operative interference. He excised the strictured region and passed a rubber tube through the distal and proximal portion of the



Fig. 18. Skin flap from thigh covering right testicle and area of scrotum.

urethra and across the perineal gap. He found that, in from 8 to 10 days, epithelialization of this bare area had occurred over the tube thus forming a new urethra.

In hypospadias, the external urethral opening is on the ventral aspect of the penis or even as far down as the perineum. Correction of this developmental defect requires the building of a new canal through the penis which will communicate with the lower end of the urethra already present. Many articles on this subject have appeared and have been reviewed by both Godard and Heynen.

The external genitalia and perineum may be injured in many ways. Falls astride horse man-hole covers, from horseback astride fences, from masts of ships, and in many other situations produced a blow on the perineum, generally ruptured the fixed urethra. Peculiar falls, which cause the clothing and the skin of the penis to be caught or in which rotating or projecting machinery causes the external genitalia to be caught, may strip the skin of the penis and the scrotum and remove one or both of the testicles. Malicious disfigurement of the penis or scrotum has produced difficult problems. Benedict's patient lost most of the skin of the penis through short circuiting of a high voltage electrical current passing through his body.



Fig. 3. Pedicle of thigh flap for scrotum sutured.

Blows to the penis when in state of erection may fracture that organ—the tunica albuginea of the corpora cavernosa is torn and a marked extravasation occurs (1, a). Strong chemicals introduced into the urethra for medical purposes may produce gangrene of the urethra and the adjacent tissues (Mallard). Automobile accidents may produce any variety of perineal and genital injuries.

#### SYMPTOMS

The trauma is usually severe and the patient may at first be in shock. There may be an associated pelvic fracture. From the penis itself bleeding is profuse. Marked pain occurs and the patient is unable to void. Leakage may occur in the proximal segment of the torn urethra.

The extent of the penile damage is noted on inspection. Several days after the injury, necrosis and sloughing of damaged tissue reveal the full extent of the loss of substance that will require replacement.

#### DIAGNOSIS

Hemorrhage must first be checked. The wound must then be treated as any lacerated wound, depending largely on the amount of foreign material present and the extent to which it is embedded in the tissue. The urinary stream must be diverted either through catheter or by suprapubic cystostomy. Where the penile injury is the site of rupture, a urinary fistula is inevitable. With

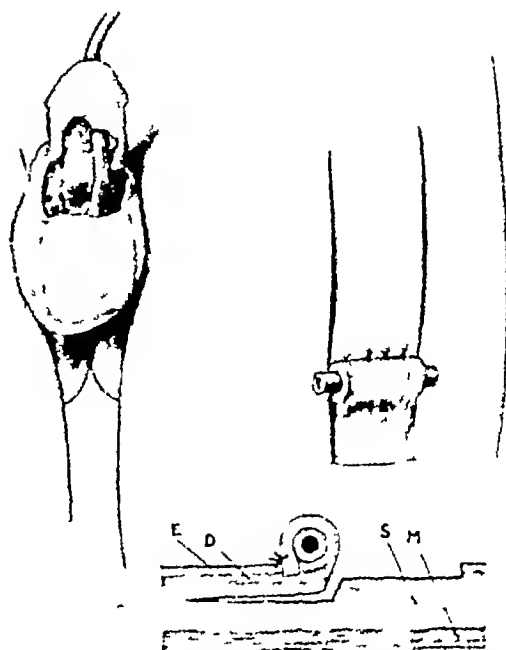


Fig. 4. Formation of tube from skin of thigh by rolling skin around catheter at distal end of thigh flap. Inset: Diagrammatic drawing of longitudinal section through lower end of thigh flap. *E*, Epidermis; *D*, dermis; *S*, subcutaneous tissue; *M*, muscle.

the tear in the anterior urethra, however, the proximal segment of the severed urethra is readily located and no difficulty is encountered in intro-

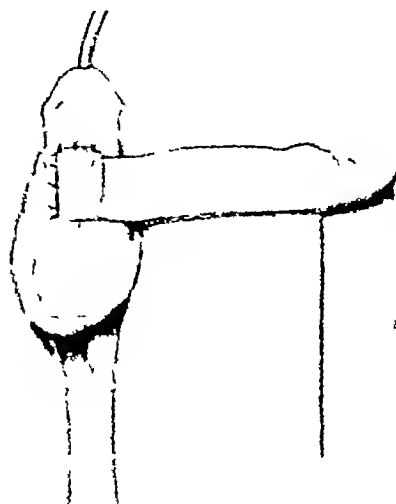


Fig. 5. Tube inserted into urethra.

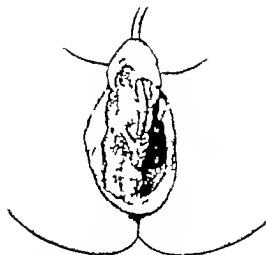


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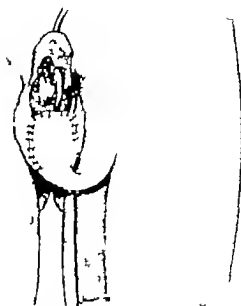


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#### TREATMENT

Hemorrhage must first be checked. The wound must then be treated as any lacerated wound depending largely on the amount of foreign material present and the extent to which it is embedded in the tissues. The urinary stream must be diverted either through a catheter or by suprapubic cystostomy. When the posterior urethra is the site of rupture suprapubic drainage is preferable. With

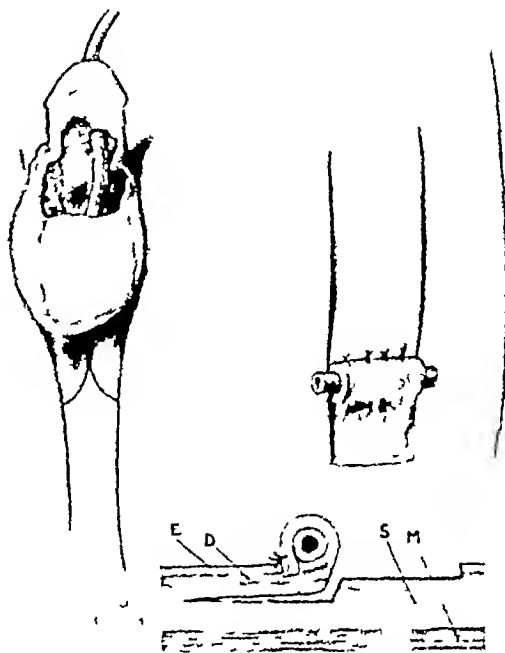


Fig. 4. Formation of tube from skin of thigh by rolling skin around catheter at distal end of thigh flap. Insert. Diagrammatic drawing of longitudinal section through lower end of thigh flap. E, Epidermis; D, dermis; S, subcutaneous tissue; M, muscle.

the tear in the interior urethra however the proximal segment of the severed urethra is readily located and no difficulty is encountered in intro-

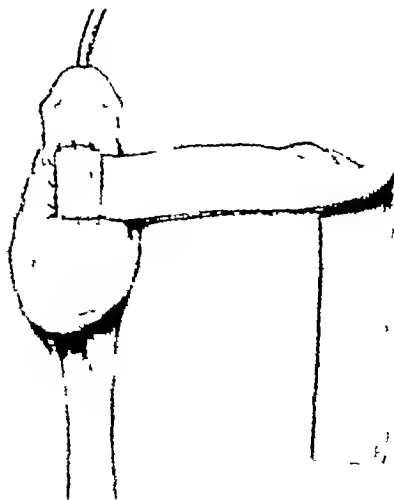


Fig. 5. Tube sutured into penile urethra.

March 6, 1938. The pedicle as cut. The freed edges are sutured with silver wire.

March 3, 1938. A few new sutures are placed here some gaping had occurred.

March 30, 1938. A single suture placed to close gap along point of the graft margin.

April 1, 1938. A urinary fistula the size of match head as still present at the peno-scrotal junction. A single pinch graft as placed in the opening.

Throughout the course of this repair, retention catheter as employed, to keep the lumen of the urethra open and allow guide for any epithelialization that might occur. On April 8, the catheter as removed, as the patient voiding through the external rectal orifice, with tiny urinary fistula at the peno-scrotal junction.

April 9, 1938. All sutures are removed. A white gauze dressing as applied.

April 21, 1938. Patient discharged from the hospital.

The patient carried on normal activities, voiding through the newly constructed urethra without difficulty. Digital pressure over the tiny fistula at the peno-scrotal junction controlled leakage while voiding.

On May 5, 1940, the patient as re-admitted to the hospital, and on May 6, 1940, under cyclopropane anesthesia, the epithelialized walls of the fistula are denuded by trousseau edge shaped incisions, the underlying granulation and subcutaneous tissues are brought together tightly with its layers of fine interrupted chromic No. 10 sutures, and a soft rubber catheter as inserted through the urethra into the bladder.

May 9, 1940. The wound as dry and the catheter as removed. Patient finally discharged from hospital on May 31, 1940.

July 8, 1940. Voiding is normal, and there is no leakage. There is no evidence of stricture. Due to the age of the patient, no definite statement can yet be given as to the ability of the repaired penis to undergo successful erection. Development of the penis in size and shape is progressing normally.

Search of the literature reveals very few case reports of restoration of penile urethra following trauma. The surgeon faced with such a problem has little to guide him, and even after a fairly extensive study may fail to find the few cases that have been reported.

To restore the urethra, we found pedicled skin tubes from the thigh and a sliding skin graft from the groin, each partially successful. A broad base must be given to the pedicle and sharp tension of the flap must be avoided. Pinch grafts, employing successful take as the source of a new graft and an amniotic preputial graft failed to repair portions of the urethra. A split skin graft from

the thigh satisfactorily supplied an outer covering for the penis. A full thickness thigh pedicled graft successfully covered the scrotum and penileum.

Great patience and persistence in repairing partial failures is necessary to attain an ultimately good result.

#### SUMMARY

The traumatic loss of 1 1/2 inches of penile urethra in a boy of 8 is reported. Adjacent portions of the penis, penile skin, scrotal skin and one testicle, were also lost. The pedicle flaps from the skin of the thigh and a sliding skin graft from the groin were employed to restore the urethra, with an ultimate good anatomical and physiological result. Reports of traumatic loss of urethral substance in modern literature are rare. Further reports are desirable to improve the technique of repair.

#### REFERENCES

- BURDET, L. H. Fracture of the penis. *Urol & Gynaecol Rev.* 1934, 30, 55.
- BRIDGES, S. K. Scrotal skin graft in severe injuries of the penis. *South M J.* 1938, 439.
- COTTELL, G. F. A rupture of scrotum, left testicle and sheath of penis. *U S Nav M Bull.* 1934, 20, 457.
- CHALLOCK, J. H. Rupture of the urethra. *Surg Gynecol & Obstet.* 1926, 37, 533-537.
- COUDARD, H. Les uréthralplasties (revue générale de procédés et de rétroplasties utilisant les transplantations libres ou pédiculées dans la restauration des hypospadias ou des pertes de substance de l'urètre masculin). *J d urol.* 1936, 42, 512.
- GOLDSTEIN, A. E. Surgical complications in the treatment of gonorrhea (indications and methods). *J Am M A.* 1935, 61, 800-804.
- HARVEY, U. Plastic repair of urethral defect. Its systematic application to penile and hypospadias. *Zeitsch f Urol.* 1931, 25, 328-359.
- MILLARD, R. S. Reconstruction of urethra and penis following extensive gangrene. *J Am M A.* 1934, 99, 337-339.
- MICKA, H. W. and HAN, C. A. Traumatic fracture of penis. *J Am M A.* 1935, 97, 105.
- MILBY, K. L. Malicious amputation of penis. *J Am M A.* 1929, 58, 855.
- LOS RANDEZ, B. Traumatic removal of entire extensor covering of penis with subsequent partial necrosis of urethra. Plastic repair case. *Zeitsch f Urol.* 1934, 28, 369-373.





March 6, 1938 The pedicle as cut. The freed edges are sutured with silk on fire.

March 2, 1938 A few new sutures are placed here some gaping had occurred.

March 29, 1938 A single suture is placed to close gaping point of the graft margin.

April 1938. Urinary fistula the size of match head as still present at the peno-crotal junction. A single pinch graft was placed in the opening.

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April 9, 1938 All sutures are removed. A cellulose gauze dressing as applied.

April 1938. Patient discharged from the hospital.

The patient carried on normal activities, voiding through the newly constructed urethra without difficulty. Digital pressure over the iliac fistula at the peno-crotal junction controlled leakage while voiding.

On May 3, 1940, the patient as re-admitted to the hospital, and on May 6, 1940 under cyclopropane anesthesia, the epithelized walls of the fistula are denuded by transverse edge shaped incisions, the underlying granulation and subcutaneous tissues are brought together tightly with layers of fine interrupted chronic No. 5 sutures, and a soft rubber catheter as inserted through the urethra into the bladder.

May 9, 1940 The wound as dry and the catheter as removed. Patient finally discharged from hospital on May 3, 1940.

July 3, 1940 Voiding is normal, and there is no leakage. There is no evidence of stricture. From the age of the patient, no definite statement can yet be given as to the ability of the repaired penis to undergo successful erection. Development of the penis in size and shape is progressing normally.

Search of the literature reveals very few case reports of restoration of penile urethra following trauma. The surgeon faced with such a problem has little to guide him, and even after a fairly extensive study may fail to find the few cases that have been reported.

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#### REFERENCES

1. BARTZ, L. H. Fracture of the penis. *Urol. & Gynec. Rev.* 1934, 30, 58.
2. BRIDGES, S. K. Scrotal skin graft in severe injuries of the penis. *South. M. J.* 9, 8, 435.
3. COTTER, G. F. Avulsion of scrotum, left testicle and sheath of penis. *U. S. N. M. Bull.* 1934, 30, 457.
4. GALLAGHER, J. H. Rupture of the urethra. *Surg. Gynec. & Obst.* 9, 3, 37, 533-537.
5. GODDARD, H. Les antrostomies (revue générale des procédés d'antrostomie utilisant les transplantations tissulaires ou pédonculaires dans la restauration des hypospadias ou des pertes de substance de l'antérieur urétral). *J. d'Urol.* 1936, 42, 107-12.
6. GOLDSTEIN, A. E. Surgical complications in the treatment of gonorrhea (indications and methods). *J. Am. M. Ass.* 1935, 64, 800-804.
7. HENRY, U. Plastic repair of urethral defect. A special attention to penile hypospadias. *Ztschr. f. Urol.* 1934, 30, 355-359.
8. MALLARD, R. S. Reconstruction of urethra and penis following extensive gangrene. *J. Am. M. Ass.* 1930, 95, 337-338.
9. MCKAY, H. W. and HARRIS, G. A. Traumatic fracture of penis. *J. Am. M. Ass.* 1935, 95, 103.
10. MURPHY, R. L. Malicious amputation of penis. *J. Am. M. Ass.* 9, 2, 57, 858.
11. VON RUDOLPH, B. Traumatic removal of entire cutaneous covering of penis with subsequent partial necrosis of urethra, plastic repair case. *Ztschr. f. Urol.* 1935, 31, 360-373.

X-ray examination showed a chronic empyema cavity with much thickening and calcification of the pleura.

On September 20, 1937, under cyclopropane anesthesia the fourth, fifth, sixth, seventh, and eighth ribs were removed from the chondrosternal junction to the midaxillary line. Following this the patient became dyspneic and required an oxygen tent for 5 days. Drainage from the sinus gradually lessened and he was discharged on October 27, 1937, with instructions to return for further surgery when his strength was regained.

He was readmitted on the service of Dr. J. O. Bower, January 10, 1938. At this time several small fistulous openings were present in the wound and from this purulent material drained. He was transferred to the service of Dr. M. Behrend on March 9, 1938.

On March 15, 1938, under cyclopropane anesthesia the old scar and the wound sinuses were excised. A portion of the third and fourth ribs were removed together with much thickened and calcified pleura and a great deal of fibropurulent debris. The empyema cavity was found to extend under the clavicle. The wound was lightly packed with vaseline gauze and allowed to remain open. The postoperative course was uneventful.

On April 21, 1938, under evipal intravenous anesthesia the wound edges were excised and the granulation tissue around the periphery of the wound was removed. The lower angle of the wound was joined with several silkworm gut sutures. The upper portion of the wound was allowed to remain open and was lightly packed with vaseline gauze. The postoperative course was smooth.

On June 9, 1938, under evipal intravenous anesthesia further plastic excision of the wound edges was carried out (Fig. 1). The lining of the empyema cavity was found to be relatively clean. The skin edges were undermined thus exposing the pectoralis portion of the pectoralis major muscle. This was separated from its insertion on the humerus. A single suture of catgut was placed through the muscle and attached to the pleura at the apex of the empyema cavity in order to obliterate the space. Following this there remained a small pocket at the base of the empyema cavity which was filled with a portion of latissimus dorsi muscle. This too was held in place with a single suture. The wound was closed without drainage. The patient was discharged in good condition on June 21, 1938.

The patient was seen at regular intervals following operation, and on each occasion appeared to be in excellent health. On February 1, 1940 it was stated that his condition was better than it had been at any time in the past 10 years and that he had fully recovered his weight and strength. On the following day the patient was struck by an automobile and instantly killed.

This case demonstrates that a chronic infection of the pleural cavity may lie dormant for many years only to be rekindled by the onset of an acute respiratory infection. The value of repeated minor procedures is also demonstrated by this case.

**CASE 2.** J. P., aged 35 years, was admitted to the service of Dr. C. A. Hiltner at the Philadelphia General Hospital on June 10, 1938. The chief complaint on admission was cough and pain in the right chest.

Five months before admission the patient had begun to notice a lightly productive cough which had become increasingly severe and productive of 2 to 4 ounces of thick yellowish sputum daily. Two months before admission he had gone to a doctor complaining of severe right lower chest pain aggravated by cough. In the past 4 weeks he had lost 10 pounds in weight and for 3 weeks had had night

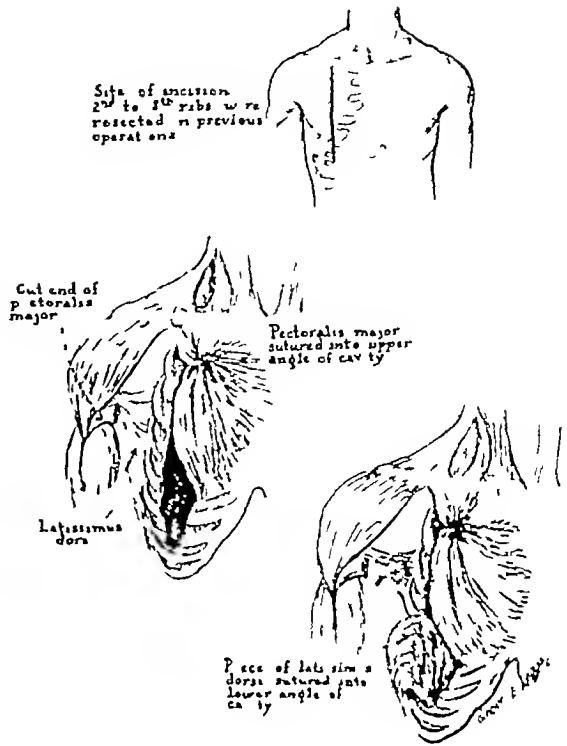


Fig. 1. Case 1.

sweats. The past medical history was that of typhoid fever in 1914. In 1928 the patient had right-sided pleurisy with pneumonia which was complicated by empyema, requiring surgical drainage. The family history was negative except for the fact that one sister of the patient has had pulmonary tuberculosis for 6 years.

Physical examination on admission revealed a fairly well nourished colored male. He was not acutely ill. However the temperature was 101.6 degrees F., pulse 96, respiration 26, blood pressure, 126/82. Physical examination was generally negative with the exception of the chest. This was fairly well developed and symmetrical. In the region of the seventh and eighth ribs posterolaterally there was a broad 3 inch keloidal scar. Expansion lagged and was decreased in extent on the right side.

X-ray examination revealed a loculated empyema on the right side with probable bronchopleural fistula.

On June 16, 1938 the right chest was tapped and approximately 400 cubic centimeters of thick pus was withdrawn. One hundred cubic centimeters of azoic bromide solution was injected. Pus from the empyema cavity showed *Staphylococcus aureus*. The sputum was negative on four occasions for tubercle bacilli. On June 17, 1938, methylene blue was injected into the pleural cavity and the patient's sputum became stained with the dye.

On June 20, 1938, under cyclopropane anesthesia the old scar was excised. Regenerated portions of the seventh and eighth ribs were removed (Fig. 2, 1 and 2). The pleural cavity was entered and approximately 600 cubic centimeters of thick greenish pus was aspirated. A definite bronchopleural fistula was exposed. The wound was lightly packed with vaseline gauze and was not sutured. The postoperative response was good.

the anesthetic must be chosen with due regard to the presence or absence of a bronchial fistula.

#### BRONCHOPLEURAL FISTULA

A most serious complication of chronic empyema is bronchopleural fistula. Such a fistula may be the chief factor in maintaining the chronicity of an empyema cavity. Pool and Garlock name pulmonary tuberculosis, lung abscess, bronchiectasis, foreign body actinomycosis, and gangrene of the lung as additional causes of fistula. The diagnosis of bronchial fistula is usually not difficult.

Bronchial fistulas may close without operation. However operation is almost always necessary to secure closure of all but the smallest bronchial fistulas. Healing is impeded by infection which commonly accompanies the fistula. When epithelialization of the sinus occurs another factor favoring chronicity is added. Several surgical methods of closing bronchial fistulas have been advocated. A most satisfactory plan is that in which a pedicle muscle flap is sewed directly into the fistulous opening. This method is illustrated in reports of Cases 2 and 3 and in the artist's sketches.

#### ANESTHESIA

Cyclopropane we have found to be a satisfactory anesthetic in operations on chronic empyema cavities. It allows administration of a good anesthetic together with a high oxygen intake, and respiratory effort is minimal. When the empyema is complicated by the presence of a bronchial fistula intravenous sodium pentothal with supplementary oxygen is the anesthetic of choice. In such cases suction through an intra-tracheal catheter should always be available to aspirate blood or pus which may find its way into the bronchi of the lung not operated upon.

#### THE VALUE OF STAGED OPERATIONS

Many years ago Robinson soundly warned of the dangers of prolonged operations and attempts to obliterate an empyema cavity in one stage. Three unroofing operations of 30 minutes at intervals of several weeks are preferable to one operation lasting 90 minutes. The manner in which empyema cavities decrease in size between stages of unroofing is often remarkable. The ultimate amount of rib removal necessary to effect complete closure is therefore less following operation in stages than if an attempt were made to remove the entire roof of the empyema cavity at one time. Between operative stages daily irrigations with saline or arochloramide solution is advisable. They help to clean up the cavity and prepare the

field for successful transplantation of pedicle muscle flaps at the final operation.

Additional conservation of rib is obtained by the use of pedicle muscle "fills." The latissimus dorsi, trapezius and pectoralis major are the muscles most commonly employed, depending on the location of the empyema cavity. However such transplants can be expected to be successful in only relatively clean cavities. This would contra-indicate their use at the first stage of most operations. We have encountered no serious loss of function in cases in which pedicle muscle grafts have been used. Care is taken to sew the muscle into the apex of the empyema cavity. Such a maneuver prevents the formation of residual pockets and also gives the transplanted muscle a new point of insertion. In the presence of bronchial fistula a portion of the muscle graft is sewed directly into the fistula opening.

#### CASE REPORTS

Three typical cases of unusual interest are presented with descriptions of the operative procedures employed. The first is a case of uncomplicated chronic empyema.

**CASE 1.** R. M., aged 3 years, was admitted to the Philadelphia General Hospital August 10, 1937 on the service of Dr. P. J. McCarthy. The chief complaint on admission was draining sinus in the left chest. The family history was negative. He had been employed as mover and carpenter.

The patient had had pneumonia 3 years before admission which was followed by an empyema in the left chest. He was operated upon at that time in another hospital and rubber tube was inserted between the ribs and allowed to drain for 6 to 8 weeks. Drainage gradually diminished and finally ceased after about 1 year. He returned to work but never regained full strength and had always been dyspneic on moderate exertion and susceptible to colds.

In January 1937 the patient had severe chest cold and cough which was productive of slim fluid expectoration. During the second week of January 1937 he developed severe pain in the left axilla and during coughing spell his left chest broke open at the site of the old incision and began to drain very foul thick yellow pus. On culture this showed *Staphylococcus aureus* and no tubercle bacilli were found. The drainage persisted and on admission measured about 6 ounces each day. He had lost 20 pounds in weight and had to stop work months ago.

On physical examination at the time of admission the patient was acutely ill. The temperature was 100 degrees F., pulse rate, 95 and respiratory rate 25. The blood pressure was 90/75. The trachea was deviated to the left. A small scar with an opening lined by granulation tissue was noted in the left anterior axillary line at the seventh interspace. The entire left chest was diminished in size and the interspaces were close together. Scoliosis to the opposite side was noted. There was very little movement of the left chest and on respiration diaphragmatic motion could not be demonstrated on that side. On percussion the entire left chest was dull. Chubb of the fingers was moderately severe.

tion At the age of 19 she developed pleurisy with left upper chest pain, fever, cough, and foul expectoration At the age of 20 she had a similar attack When 24 years of age she was told that she had an abscess of the lung and was operated upon elsewhere for this Since then she had had 8 additional operations on the chest together with a left phrenic eversion, all done elsewhere At these operations apparently considerable lengths of several ribs had been removed Despite this the patient continued to cough and expectorate about 4 ounces of foul sputum daily There had been considerable drainage through a sinus in the chest wall The patient found it necessary to keep a rubber tube in this sinus to maintain drainage On several occasions the tube had been lost but was always coughed up through the mouth The last operation was performed 7 years ago and ever since then the bronchopleural fistula had been draining A year before this admission the patient had several pulmonary hemorrhages over a period of 2 weeks The patient's mother died of cancer of the breast, and her father died of cancer of the esophagus One brother died of diphtheria, while another brother and two sisters are living and well The patient is unmarried and unemployed She has always been ill and has shunned society because of sensitiveness about the odor of the drainage

The patient was not acutely ill on admission The temperature was 99 degrees F, pulse, 80, respiration, 22, blood pressure, 130/70 Examination of the chest showed dullness at the left base posteriorly Opposite the angle of the scapula a deep depression with a hole through the chest wall in which a rubber tube is inserted was observed Four scars of previous operations on the left chest were noted

On March 25, 1939, operation was carried out under intravenous pentothal anesthesia with the patient lying on the right side The fistulous tract was explored and widened A small chronic empyema cavity was entered at the upper angle of which there was a bronchopleural fistula opening about the size of a lead pencil There also appeared to be several smaller fistulas below this The empyema cavity appeared to be relatively clean and had been thoroughly unroofed as a result of the previous operations Therefore, it was decided to attempt closure of the fistula opening by means of a pedicle muscle graft at this time However, the latissimus dorsi and trapezius muscles had been largely destroyed and replaced by fibrous tissue as a result of the previous operations (Fig 3) It was therefore necessary to use a piece of the erector spinae muscle group which was fashioned into a pedicle graft about 2 inches thick A suture was taken in the freed end of the muscle and this in turn was sewed directly into the fistula opening Additional interrupted sutures were taken in the muscle flap to hold it securely in the chronic empyema cavity The skin was closed by means of interrupted black silk sutures without drainage

On March 30, 1939, these sutures were removed and there was a moderate amount of drainage from the wound Following this the wound was irrigated daily with 1 to 10,000 potassium permanganate solution On April 10, 1939, the patient was discharged At this time the wound was practically healed, and drainage was very slight She was seen in follow up clinic in April, 1940 The operative wound was entirely healed Cough had disappeared and there was at the most 1 to 3 drams of sputum raised in the

morning but lately even this is occasionally absent The patient is acquiring an entirely new outlook on life and psychologically is now able to take her place in society

This case is of interest in view of the many previous operations which had failed fully to obliterate the empyema cavity and to close the bronchopleural fistula The fact that the patient occasionally lost the drainage tube which was subsequently coughed up is also unique The long history of pulmonary infection might have led to a rather diffuse bronchiectasis, but the post-operative course has given no reason to believe that it exists

#### SUMMARY

1 The factors on which the successful surgical treatment of chronic empyema depend have been discussed

2 The value of multiple staged operations in the treatment of chronic empyema has been noted The combination of pedicle muscle transplants with partial selective thoracoplasty has been advocated because it conserves ribs and produces a minimum of deformity

3 Problems introduced by the presence of bronchial fistula in chronic empyema cavities together with a satisfactory method of treatment, are also discussed

4 Three illustrative case histories have been included

#### BIBLIOGRAPHY

- 1 CARTER, B N The use of muscle flaps in the closure of chronic empyema cavities *Surgery*, 1938, 3 506-517
- 2 DÉLORME, E On traitement des empyemes chroniques pour la dicortication du poumon 10 *Congres de Chir, Par*, 1896, p 379
- 3 LIGGERS, C Radical operation for chronic empyema *Ann Surg*, 1923, 77 327
- 4 GRAHAM, L A Principles involved in the treatment of acute and chronic empyema *Surg, Gynec & Obst*, 1924, 38 466-470
- 5 GRAY, H K The use of pedicle muscle grafts in facilitating obliteration of large chronic non tuberculous pleural empyema cavities *Minnesota Med*, Sept 1938, 21 608-610
- 6 KIRSCHNER, O Zur Radikalbehandlung des chronischen Pleuraempyemas *Arch f klin Chir*, 1921, 117 205
- 7 MELCHIOR, F Das Pleuraempyema, *Beitr z klin Chir*, 1920 145 543
- 8 POOL, L H and GARLOCK, J H A treatment for persistent bronchial fistula *Ann Surg*, 1929, 90 213-237
- 9 ROBINSON, S The treatment of chronic empyema *Surg, Gynec & Obst* 1916 22 557 571

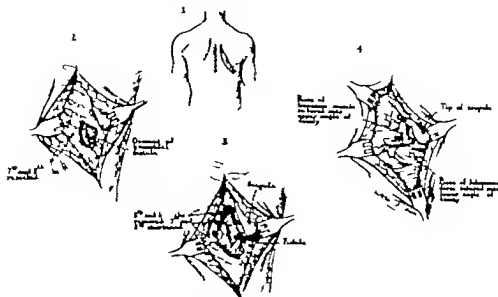


Fig. 2. Case 2.

On July 26, 1938, under intravenous cervical anesthesia the old incision was extended to allow resection of the fifth and sixth ribs overlying the chronic empyema cavity. The posterior stamps of the seventh and eighth ribs were also shortened (Fig. 2). Thickened parietal pleura and intercostal muscle bundles of the fifth and sixth ribs were removed. The wound was tightly packed with vaseline gauze and partially closed with through-and-through line sutures. The postoperative course was uneventful. Following this stage, the drainage was greatly decreased.

On August 30, 1938, under cervical intravenous anesthesia plastic removal of granulation tissue in the scar was carried out and the remaining portion of the empyema cavity was unroofed. The wound was packed lightly with vaseline gauze and was not sutured. The postoperative course was uneventful.

On November 3, 1938, under cyclopropane anesthesia the scar of the previous operations was excised. The skin was reflected backward on each side of the incision. The remaining empyema cavity was about the size of a hen's egg. In the small amount of pus which was present air bubbled periodically with respiration. A piece of trapezius muscle was detached at one end from the main body of the muscle and sutured into the cavity as a pedicle graft (Fig. 3, 4). Since this did not fill the cavity, similar procedure was carried out using pieces of latissimus dorsi muscle. The muscle was sutured all up into the spot of the empyema cavity and care was taken to sew it directly into the fistulous opening. The wound was closed with interrupted silk suture sutures. Convalescence was uneventful and the patient left the hospital weeks after operation. He has returned to his occupation as chief and reported in February 1940, that he was perfectly well.

This case demonstrates the value of repeated small unroofing plastic operations in the surgical treatment of chronic empyema. The value of pedicle muscle grafts in the treatment of chronic empyema and bronchopleural fistula is also demonstrated. Undoubtedly their use in this case shortened the period of disability and enabled the patient to return to work in a minimum time.

CASE 3. M. H., aged 33 years, was admitted to the Jewish Hospital March 1930. Her chief complaint at admission was draining sinus in the left chest. At the age of 4½ years the patient had had paronychia, and ever since that time there had been some cough and expectoration.

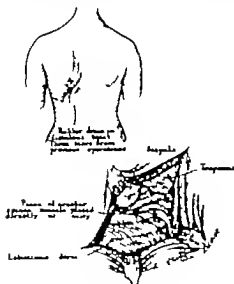


Fig. 3. Case 3.

the incision apart, their contraction does not produce pain. These same muscles are the ones primarily concerned in coughing, therefore, the patient has less dread of expectorating. The combination of relatively painless motion, respiration, and coughing leads one to expect a very low occurrence of pulmonary complications.

For those patients who judge the merits of an operation by the appearance of the scar, this incision is particularly desirable, the part which is not hidden by the pubic hair follows the natural

skin lines and will eventually merge with these lines.

#### SUMMARY

A transverse low abdominal incision for clean cases is described which combines the following advantages: (1) very wide exposure, (2) strength, (3) no need of muscular relaxation, (4) less inhibition to respirations postoperatively, (5) technical simplicity, and (6) good cosmetic result.

I wish to thank Dr. John B. de C. M. Saunders for his suggestions and constructive criticism.



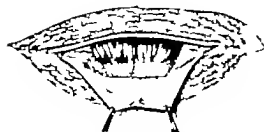


Fig. 2. A, Left: The lower flap of the rectum sheath elevated to expose the tendinous ends of the rectum. The dotted line indicates where they are to be divided. Note the fibers of the internal oblique muscle showing at either end of the



incision in the fixed aponeurosis of the oblique abdominal muscles. B, Showing suturing of the rectum to the lower flap of the rectum sheath. A second row of sutures may be inserted if desired.

larger than that afforded by the vertical incision. An additional advantage lies in having the center rather than the end of the incision over the operative field. Inasmuch as the overhanging fold of fat found in very obese persons is above the level of the transverse incision, it will not be in the way of the surgeon, thus appreciably decreasing the depth of the wound.

The exposure gives ready access to the lower sigmoid and the upper rectum, the region of the bifurcation of the aorta and the organs contained in the broad ligament (Fig. C). Even in the male, the rectum can be mobilized as far as the end of the coccyx under direct vision and without the handicap of working in a deep funnel. Surgeons who favor the preservation of the anal sphincter as in the Devine procedure for excision of carcinoma at the rectosigmoid junction, will be able to remove more of the rectum and to achieve an anastomosis deeper in the pelvis than can be accomplished with the use of the vertical incision.

The incision described is not intended for general exploration of the abdominal cavity, but it will permit palpation of the liver and the performance, if desired, of the incidental appendectomy, unless the appendix is located unusually high. Exceptionally large pelvic tumors extending to the umbilicus would also be difficult to deliver through this incision.

The strength of the abdominal wall following this approach results from 4 factors: (1) no part of the muscle is denervated—the pyramidalis is of little account; (2) the aponeuroses of the oblique abdominal muscles, the recti muscles themselves and the peritoneum are divided at different levels—in a staggered incision the layers of the abdominal wall are not weakened in the same place; (3) all the sutures are taken in tendinous structures which offer more secure anchor

age and more reliable union; (4) the direction of the pull of the oblique abdominal muscles is parallel to the direction of the incision in their aponeuroses. Consequently, the line of suture in this most important layer of the anterior abdominal wall is subjected neither to the constant strain of muscle pull nor to the sudden disrupting jerk during paroxysm of coughing. The incidence of herniation or postoperative hernia should be negligible.

The low abdominal incision is also attractive from the point of view of anesthesia. As the incision is below the level of the eleventh segment of the thoracic cord, spinal anesthesia need not extend higher; accordingly, there is less depression of the blood pressure. If general anesthesia is employed, it may be light, except when the rectus muscles are being re-attached; no muscular relaxation is required at other times because the contraction of the muscles does not tend to close the wound. The edges of the wound gape without the aid of retractors. Very little packing is required to keep the small intestines out of the field and, for this reason, there is less tendency to postoperative distention.

The lower abdomen is not used much in respiration even by men. Consequently the pain of a low abdominal wound is not aggravated by breathing and will have almost no inhibiting influence on respiration. Since the incision is relatively painless, the requirement of narcotics is diminished—pillow under the patient's knees for the first 4 days will further reduce postoperative discomfort. No adhesive strapping is needed above the iliac crests, thus further promoting better pulmonary ventilation. The surprising freedom with which the patient moves in bed after operation can be easily explained by the consideration of the anatomical factors involved: the patient is free by the use of the oblique abdominal muscles, since they do not tend to pull

the incision apart, their contraction does not produce pain. These same muscles are the ones primarily concerned in coughing, therefore, the patient has less dread of expectorating. The combination of relatively painless motion, respiration, and coughing leads one to expect a very low occurrence of pulmonary complications.

For those patients who judge the merits of an operation by the appearance of the scar, this incision is particularly desirable, the part which is not hidden by the pubic hair follows the natural

skin lines and will eventually merge with these lines.

#### SUMMARY

A transverse low abdominal incision for clean cases is described which combines the following advantages: (1) very wide exposure, (2) strength, (3) no need of muscular relaxation, (4) less inhibition to respirations postoperatively, (5) technical simplicity, and (6) good cosmetic result.

I wish to thank Dr. John B. de C. M. Saunders for his suggestions and constructive criticism.



# PRACTICAL POINTS IN THE DIAGNOSIS AND TREATMENT OF FRACTURES OF THE JAWS

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ONE of the conspicuous clinical observations in the field of traumatic injuries during the past two decades has been the increasing incidence of fracture of the maxillary bones. This fact is but a natural consequence in an economy which is characterized by a highly geared industrialism with the emphasis on speed. The all too frequent failure to diagnose correctly such fractures may be attributed in a large measure to a lack of acquaintance with the fundamental principles of treatment. That hospital administrative boards are recognizing the need for specialized handling of these fractures is evidenced by the growing tendency to appoint competent oral surgeons to the consulting staff.

## GENERAL CONSIDERATIONS

Fractures of the jaws possess the inherent possibility of serious complications. The fractured maxilla is more prone than the mandible to have associated skull or brain injuries. The most serious complication is a fracture of the base of the cranium which, besides being often accompanied by brain injury that may of itself be fatal, leaves an open avenue to intracranial infection (1). Cellulitis and osteomyelitis may develop, especially when the lower jaw is the site of injury. In order to determine properly the type and degree of injury, both a clinical and roentgenographic examination should be instituted. Since the trauma often involves contiguous structures, a digital examination of the facial bones should be made. By means of the thumb and forefinger the maxillary malar and nasal framework can be outlined. Fractures of the zygomatic arch that are obscured by swelling may often be detected by tracing the orbital borders. Particularly should there be an intra-oral inspection of the dental arches.

The most commonly observed and significant sign of fracture of the jaws is the mobility to approximate the teeth in a normal manner. Some of the other symptoms are tenderness at the point of injury, ecchymosis, mobility of the parts, and

loss of function. When the traumatizing force has been great enough, injury to branches of the fifth nerve results causing paresthesia of those areas in which it innervates. Clinical examinations should always be supplemented by roentgenographic survey. The mandible in particular lends itself to study by means of the roentgen ray. However, two lateral jaw exposures are insufficient, only when additional views of the symphysis and ramus, including the coronoid and condylar processes have been made, can the survey be considered complete and adequate for diagnostic purposes. Fractures of the maxilla are not as easily determined by the roentgenogram because of the overlapping of the cranial bones which tends to blur the fracture lines. Therefore the importance of a careful clinical examination is obvious.

## THE MAXILLA

The upper jaw is less frequently the site of fracture than the mandible. This may be attributable to the more pronounced position of the latter and to the natural protection and support afforded the maxilla by the adjacent bones. Anatomically it consists of two maxillae together forming the upper part of the face and containing the antrum of Highmore. Although frailly attached to the skull, it is strongly supported posteriorly by the frontal, the sphenoid and temporal bones. Not only do these buttresses tend to prevent injury from blows delivered from in front, but they also serve to absorb and disseminate shocks, thus alleviating the deleterious effect on the cranium.

Fracture of the maxilla may involve only the alveolar process or may be so extensive as to detach the whole jaw from the skull. When displacement is marked, it is due more to the original violence and gravity than to any muscular force. Often associated with the injury, particularly in complete transverse fractures, is fracture of the malar bone. Hemorrhage into the antrum, loosening or devitalization of several teeth and lack of sensation of parts of the face are symptoms frequently observed.

The treatment, except in oblique fractures of the maxilla, may be conveniently administered by utilizing intra-oral methods of immobilization, details of which will be discussed later. When



Fig 1 Gilmer methods of wiring a, left, No 1 method, wires crisscrossed, and joined to wires similarly arranged below b, No 2 method metal splints attached by fine wires to upper and lower arches Intermaxillary tie wires connect splints

the line of fracture runs transversely through the maxilla or higher up through the orbits, the necessity for support obtained from outside the mouth becomes apparent. In these patients the entire jaw hangs loosely by the soft tissues, the face presenting an elongated appearance. From a headcap of leather or other material, with the skull as a point of anchorage, connection is made with a metal splint previously attached to the upper dental arch. Thus, upward traction on the maxilla can be exerted which anatomically restores the natural facial contour. That the normal relation of the teeth of the upper and lower jaws should be reestablished is axiomatic and fundamental. Because deformity may result, fragments of bone should not be removed unless wholly detached, as the richly nourished maxilla tends to heal with surprising rapidity.

#### THE MANDIBLE

Of all the facial bones the mandible, although the largest and strongest, is most often fractured. Injury may occur at any point from the symphy-

sis to, and including, the condyle. The most constant site of fracture is the angle, the next most common location is the region of the mental foramen. Statistical studies have revealed that bilateral fractures usually involve both these regions (4). Fractures of the body of the mandible are generally compound, communication with the oral secretions being through lacerations of the mucous membrane or the sockets of the teeth. The majority of the edentulous cases are of the simple type, yet present mechanical problems in immobilization. Although displacement in fracture of the mandible is primarily caused by trauma, it is accentuated by the strong traction of the many muscles to which the jaw gives attachment. The anterior fragment is depressed by the suprahyoid group while the ramus is elevated by the masseter, internal pterygoid, and temporal muscles. Even the slightest displacement causes disruption of the normal articulation of the teeth. Steering-post accidents are a potential and increasing cause of injury to the condyle. Fracture of the neck of the condyloid process is

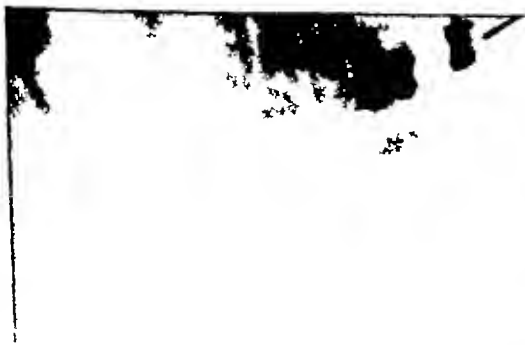


Fig 2 Fracture of mandible with displacement of ramus



Fig 3 Same case after reduction with metal splint and elastic traction



Fig. 3 Fracture of maxilla of 3-year-old boy. Reduction by means of Gilmer method.

the result of indirect force fracture of the symphysis is sometimes co-existent. Unless precluded by the direction of the fracture line the bend may be displaced from its normal position to the temporomandibular fossa. The most characteristic symptom is deviation of the chin toward the affected side. Shortening of the ramus on the same side is a logical consequence.

#### TREATMENT

The management of fractures of the jaws has for its aim the overcoming of muscular pull by restoring and maintaining the parts in proper position. When teeth are present, it is a basic rule to re-establish occlusion which requires careful and accurate reduction. The vast clinical material of the World War furnished an unusual opportunity for the study of jaw injuries. Since immobilization is mainly a mechanical problem, the choice of method should be the simplest and most effective means possible. The procedures used today are modifications of the basic ideas of Gilmer whose principles in the treatment of fractures still remain classic. The first method which he advocated consists in looping a wire around the neck of a tooth and twisting the ends together. This operation is carried out on two adjoining teeth and similarly on the occluding lowers. The wires are crisscrossed before winding the upper and lower ones together; meanwhile the occlusal relations are secured. The Gilmer second method involves the adaptation of a metal splint to the teeth of each jaw by threading fine wires around the necks of the teeth. Intermaxillary tie wires connect the splints and firmly hold the jaws in position. Because of the successful

results obtained, especially in badly displaced instances, there is an ever growing tendency today to use intermaxillary elastic traction.

These methods are equally applicable to the treatment of partial fractures of the maxilla the basic tenet of treatment which remains the same. Clinical experience has shown that the Barton and other type of head bandages are of little value except as a supplementary aid to some other form of fixation. The pressure of a bandage is inclined not only to cause pain but in some cases actually to increase displacement of the fragments. The majority of the fractures of the mandible can be treated by non-surgical means as we have illustrated. Surgical intervention is for the most part limited to certain types of edentulous cases, the management of which was discussed in detail in a previous paper (1).

The postoperative care consists in maintaining good oral hygiene giving adequate attention to the diet, and preserving the general health of the patient. Loss of weight during the early period of immobilization is a common observation. Occasional adjustment of the stabilizing devices is necessary to maintain correct alignment of the bone. Such complications as osteomyelitis and malunion can often be avoided by the maintenance of ample drainage of all suppurating areas. The usual period of immobilization is about 5 weeks (3).

#### SUMMARY

The diagnosis and treatment of fractures of the mandible and maxilla necessitate the employment of both a clinical and roentgenographic examination. A complete roentgenographic survey is essential, particularly of the lower jaw. The basic principles of treatment are predicated upon the accepted concept of restoring the normal relation of the teeth thereby satisfying both functional and cosmetic requirements. That many cases are complicated by infection, delayed union, malunion, and in some instances nonunion is attributable in a large degree to a lack of knowledge of or deviation from, the cardinal principles of treatment advocated by Gilmer.

#### REFERENCES

1. BLAIR, VERA. P. Surgery and Diseases of the Mouth and Jaw. P. 89. St. Louis: C. V. Mosby Co. 1930.
2. DOWLING, JOSEPH A. The management of fracture of the edentulous mandible. *Appl. Anatomy*, 1936, 6, 5.
3. IDEM. A statistical study of 100 cases of fracture of the mandible. *J. Am. Dent. Ass.* (in press).
4. IVE, ROBERT H. Fractures of the mandible. *J. Am. Dent. Ass.* 1927, 14, 1009.

# A STRAIGHT LATERAL INCISION FOR UNILATERAL SUBOCCIPITAL CRANIOTOMY

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SINCE craniotomies are at best time-consuming procedures, I believe it worth while to call attention to a straight lateral musculocutaneous incision that I have employed for several years in performing unilateral craniotomy. It has definite advantages over both the curved and Cushing crossbow types of incisions, since it can be made more quickly and closed more rapidly than either of the two. It affords equally as good exposure and even stronger closure, since the incision is muscle splitting rather than muscle cutting.

The incision has become of more significance since unilateral suboccipital craniotomy has become an accepted operative procedure in exploring the cerebellopontine angle. The approach is used chiefly for performing subtotal section of the eighth cranial nerve in Ménière's disease and total section of the ninth cranial nerve for glossopharyngeal neuralgia. It is also used in performing section of the trigeminal nerve and for tractotomy, and we of the Section on Neurologic Surgery are employing it more and more in operating for acoustic neuroma.

In preparing the patient for operation, I prefer to have ether administered by the drop method over a Magill tube which has been introduced into the trachea. As soon as the patient has been anesthetized I prefer the use of the cerebellar upright position (Fig. 1) to the use of the horizontal position because, if the former is used, the occipital region will be on the same plane as are my eyes during the operation. The musculocutaneous bleeding also will be much less. The use of the large intratracheal tube and the upright position prevents venous congestion and anoxemia which, in turn, reduces the intracranial pressure and eliminates the frequent need of aspiration of the lateral ventricle and the administration of hypertonic solutions. If orthostatic hypotension exists, the cerebellar upright frame will have to be tipped forward to lower the head during the operation.

## TECHNIQUE OF STRAIGHT LATERAL INCISION

After the surgical field has been prepared and draped, the following structures are identified, the

1 from the Section on Neurologic Surgery, the Mayo Clinic.

mastoid prominence, the superior occipital ridge, the external occipital protuberance and the lateral border of the trapezius muscle. The incision begins 3 centimeters to the right or left of the occipital midline and 2 centimeters above the superior occipital ridge. It is then extended downward into the neck to a point opposite the spine of the axis. The incision, though straight, takes a lateral course to end between the trapezius and the sternocleidomastoid muscles, but does not incise the splenius capitis and cervicis muscles. The incision is made to extend through the scalp, fibers of the occipitalis and transversus nuchæ muscles, and periosteum.

Bleeding of the scalp is controlled by digital pressure until the scalp hemostatic clips are applied. The occipital artery and veins are ligated with catgut. The smaller vessels are electrocoagulated. The occipital bone is exposed by freeing and retracting the periosteum and muscles *en masse*. Unilateral craniotomy from this point may be extended in any desired direction (Fig. 2a). In exploring for tumors of the cerebellopontine angle I prefer to extend it toward the midline in order to decompress the medulla oblongata and to elevate the cerebellar tonsils, if such exist (Fig. 2b).

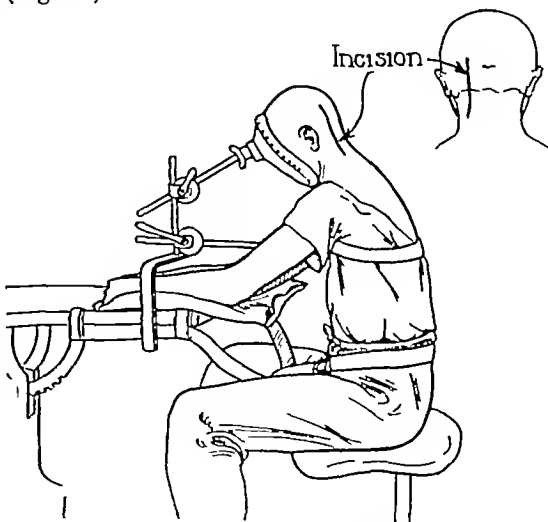


Fig. 1 Cerebellar upright position

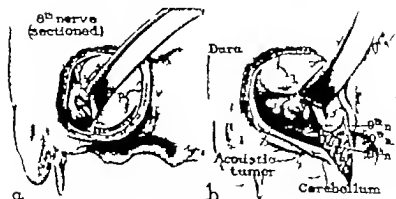


Fig. a, Unilateral suboccipital craniotomy (section of eighth cranial nerve) b, unilateral suboccipital craniotomy (exposure of acoustic tumor)

#### CLOSURE OF THE INCISION

A continuous suture of No. 1 catgut can be used in closing the muscle planes, since they have been split rather than incised. The one exception is the small transversus nuchae muscle. The fascial planes superficial to the muscles and the periosteum cephalad to the muscles and galea are closed with interrupted sutures of silk. The dermal closure may be of continuous or interrupted

silk sutures. The dressings used are those of steril gauze fastened with adhesive. The muscle splitting incision is much less painful after operation than the transmuscle section incision. The patients are permitted to lie up and about on the third postoperative day and they are allowed to move the head and neck as much as they please without any fear of the incision being torn open.

# HAMMER-TOE

## A New Procedure for Its Correction

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**A**LTHOUGH many operations have been devised for the correction of hammer-toes, the most generally used procedure is a simple wedge resection of the proximal interphalangeal joint. Following this operation the toe must be splinted in the corrected position approximately 6 weeks for bony fusion to occur. Jones advises a wedge shaped resection of the joint with the base upward, division of the flexor tendon, and fixation of the toe to a splint. He advises that the patient walk about, wearing the splint on the inside of his boot in order to make sure that solid ankylosis occurs without any return of the deformity. However, it is difficult to splint a toe properly while the patient is in bed and much more difficult to splint efficiently the toe of an ambulatory patient. One cannot ask a patient who has had the relatively minor operation of correction of a hammer-toe to remain in bed for 6 weeks. If, through faulty immobilization, fibrous ankylosis occurs, the result may be clinically satisfactory, but there is always the danger that the deformity may recur.

Many surgeons have attempted to improve, by various devices, the methods of splinting in common use. Lake advised the application of a splint of stout iron wire bent to fit the parts. He advised that this be kept on for 2 weeks after which strapping may be used as a substitute. Trethowan advised collodion and gauze-strip dressings, changed every 2 weeks for a total of 6 weeks. Creer devised an ingenious fork-like splint of duraluminum which fitted on the dorsum of the

foot but divided at the cleft of the toe into the two lateral prongs to which the toe was bandaged.

It has been suggested that a silk suture be placed about the proximal phalanx at the time of operation and brought out through the plantar surface of the toe where it could be tied about a plantar splint. This proved impractical in my hands, as the immobilization was not satisfactory, both the suture and the splint moving about when the patient walked.

Several operations were devised with the express purpose of obtaining internal splinting.

I was impressed by an ingenious, but rather complicated, operation described by a French orthopedist, Tierney. He used the principle of spiking the distal end of the proximal phalanx into a rotated portion of the phalanx itself in an attempt to maintain correction without splinting. I attempted the procedure several times, but had difficulty in maintaining the spike in its socket.

Young and Higgs independently described a less complicated spike operation which offered the same difficulty as the Tierney procedure. I found it difficult to obtain and maintain a snug fit of the spiked end of the proximal phalanx in the cavity in the middle phalanx.

In an attempt to obtain a more satisfactory method of splinting, I devised an operation that permits efficient immobilization in the corrected position in an ambulatory patient. In some cases the patient was operated upon and permitted to walk the next day in a cut-out shoe. Unless there are contractures of the metatarsophalangeal joint

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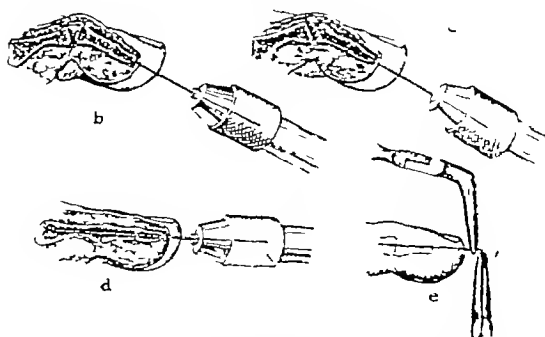
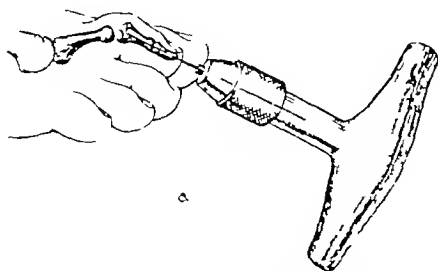


Fig. 1 a Schematic drawing of the wire, the chuck and its method of insertion after the proximal interphalangeal

joint has been resected b to e, Schematic drawing of the subsequent steps in the operation



Fig. 2, left. Showing the postoperative position of the wires on anteroposterior and lateral projection in Case 1 of 5. Bony union in the corrected position in Case 5.

to be overcome by capsulotomy or tenotomy the patient need not stay in the hospital after the operation. I have performed the operation on 20 toes in 10 individuals in the past 6 months and the results have been satisfactory. While the period is too short for a long term follow-up bony union was obtained in all the cases in which the procedure was properly carried out. Local or general anesthesia may be used, according to the indications. If local anesthesia is used, it is unwise to use a tourniquet about the base of the toe because of the remote possibility of gangrene following the combination of local anesthesia and tourniquet as described by Garlock.

Through a medial longitudinal incision over the proximal interphalangeal joint the articulation is exposed. A transverse incision may be used if desired and is especially satisfactory if heavy corn is present over the joint, as this can then be excised by an elliptical transverse incision. Theoretically the longitudinal incision is less likely to interfere with the blood supply of the toe but in many toe operations for other conditions I have seen no circulatory disturbances following a transverse incision. No circulatory difficulties occurred in the present series of cases in which the average age was 38 years and ranged from 11 to 64 years.

The cartilage is then carefully and completely removed from the opposing articular surfaces, preferably with a small osteotome and curette and this usually permits correction of the deformity. If the angulation cannot be readily corrected, bone should be removed from the proximal phalanx. Remove merely enough bone to obtain correction of the angulation but do not resect too much bone. Ravity is to be avoided. Because the smallness of the middle phalanx makes it difficult to carry out the procedure it is outlined, as little bone as possible should be removed from this part. Any deformity of the distal joint can be corrected by manual stretching. A Kirschner wire, 35/1000 of an inch thick (Fig. 18) is then inserted, by means of a hand chuck, longitudinally through the tip of the toe through the distal phalanx, through the distal interphalangeal joint and through the middle phalanx until the point of the wire appears at the denuded proximal surface of the middle phalanx. If the bones are unusually large a wire 45/1000 of an inch thick should be used. The wire is inserted by a rotary movement of the chuck. Strong pliers must be used to fasten the wire in the chuck or it will tend to rotate in the chuck rather than penetrate the bone. It takes some



Fig. 4 Postoperative position of the wires in Case 2 Bilateral anteroposterior and lateral views

practice to insert this wire correctly even under direct vision, and if the point of the wire does not appear approximately in the center of the denuded surface of the middle phalanx, another attempt should be made. In some cases three or four attempts were necessary before the wire was properly centered. No ill effects followed the multiple passages of the wire, and motion in the distal interphalangeal joint was only slightly or not at all impaired after the withdrawal of the wire 6 weeks later. If the point of the wire appears at the denuded proximal surface of the middle phalanx, the chuck is carefully released with the aid of pliers to avoid the inadvertent disturbance or withdrawal of the inserted wire. An additional length of wire, corresponding to two thirds of the length of the proximal phalanx, is now permitted to extend from the chuck. The length of the average adult proximal phalanx of the second toe is between 1 inch and  $1\frac{1}{4}$  inches. Therefore, if approximately  $\frac{2}{3}$  of an inch of wire is inserted into the proximal phalanx sufficient immobilization is obtained and there is no danger of crossing the metatarsophalangeal joint. If the operation is carried out on the other toes,

the surgeon must, by clinical and x-ray measurements, estimate the length of wire to be inserted into the proximal phalanx (Fig 1b).

Carefully, to avoid disturbing the partially inserted wire, the chuck is again tightened with pliers, and the point of the exposed wire is then carefully placed at the center point of the denuded distal surface of the proximal phalanx (Fig 1c). This position of the point of the wire is maintained, the deformity is corrected, and the wire is driven longitudinally through the proximal phalanx by the same rotary motion of the chuck (Fig 1d). If, by any chance, the wire is not centrally placed in the proximal phalanx, it should be carefully withdrawn until the point again protrudes from the middle phalanx, and the procedure repeated. If the operator is satisfied that the wire has been satisfactorily driven, the resected joint should be inspected. The joint must be flush and the two phalanges firmly fixed to one another without any intervening space. If motion between the two phalanges can be demonstrated, one can be certain that the wire has not been properly placed. By means of two small right angle pliers the projecting end of the wire



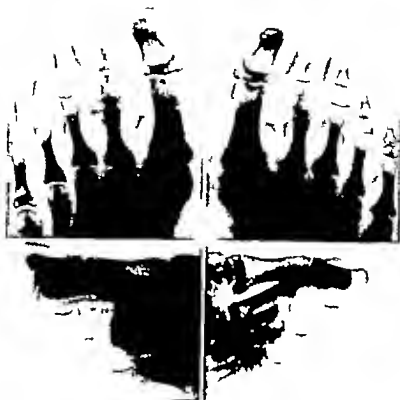


Fig. 5. Union in the corrected position in Case . . . Bilateral anteroposterior and lateral view.

should be carefully bent to a right angle and the excess wire cut off (Fig. 1c). This last step is to prevent the possibility of the wire wandering deeply into the tissues. I have experienced no wandering of the wires except in those cases in which the wire had entirely crossed the metatarsophalangeal joint. A small longitudinal strip of gauze is now placed over the wound extending around the end of the toe to the plantar surface and the projecting end of the wire is permitted to extend through the gauze. Collodion is used to fasten the gauze to the skin and a further dressing is necessary except two small strips of adhesive over the projecting end of the wire to prevent its catching in objects. It is wise at first, to have an x-ray check-up before the patient is discharged. If the x-ray examination shows that the wire has been satisfactorily placed, the patient may be discharged immediately to resume normal activities with the use of a cut-out shoe. If no pain or temperature occurs, the wire and the sutures may be removed at the same time in 6 weeks. If pain or swelling occurs, the wound

should be inspected, at which time the sutures can be withdrawn. In the series thus far there have been no infections. In four toes there was a slight serous discharge about the wire which was somewhat loose. In 2 of these cases the wire had been permitted to cross the metatarsophalangeal joint and I think the resultant motion of the wire when the patient walked caused the serous discharge. The wounds rapidly closed as soon as the wires had been withdrawn.

CASE J. H. male, aged 35 years, for many years had badly deformed second, third, and fourth hammer toes on the left foot. Under local anesthesia on January 30, 1930, the procedure described was carried out on the second, third, and fourth toes. Postoperatively roentgenograms (Fig. 6) showed satisfactory position of the wires. The exception of the fourth toe in which the wire crossed the metatarsophalangeal joint. The patient was discharged 4 days later and allied about with cut-out shoe. A month after the operation the sutures were removed and primary union of all the wounds noted. Four weeks later the wires were withdrawn. There was slight swelling and serous discharge about the wire in the fourth toe for the reason noted. This rapidly subsided, and the wire openings promptly closed. Roentgenograms

9 weeks after operation (Fig. 3) showed solid bony union, and the patient has had no further disability.

The method has been used on all toes except the great toe and has been found equally efficacious in the correction of congenital hammer-toe deformities.

CASE 2 N I, female, aged 11½ years, had bilateral hammer toe deformity of the second toe since birth. Under gas oxygen ether anesthesia the operation described was carried out. Special care was taken to remove a thin layer of cartilage from the proximal end of the middle phalanx to avoid, if possible, interference with the epiphysis (Fig. 4). The wires and sutures were removed 6 weeks later, and x ray examination revealed union in excellent position (Fig. 5). The correction has been maintained.

Contractures of the distal interphalangeal joints and the metatarsophalangeal joints are usually secondary to the main contracture at the proximal interphalangeal joints and are readily corrected by stretching. Occasionally, if the contracture at the metatarsophalangeal joint requires tenotomy or capsulotomy, this should be carried out. After the correction of the proximal interphalangeal joint and the proper application of the wire, the collodion strip can be extended on to the dorsum of the foot for 2 inches, and this will usually be sufficient to maintain the correction in the metatarsophalangeal joint. Threaded wires were not used because of the smallness of the parts, the occasional need for multiple insertions before the wire is satisfactorily placed, and because there has been no difficulty with wandering (8) of the wires.

The method is simple and direct, but it requires careful attention to detail for its successful

use. The danger of infection is apparently more theoretical than real, especially if the wires are satisfactorily inserted so that no movement occurs. Several of my patients who had previous hammer-toes operated upon and splinted by older methods were unanimous in approving of the Kirschner wire immobilization.

#### BIBLIOGRAPHY

- 1 CREER, W. S. Treatment of hammer toe. *Brit. M. J.*, 1935, 1, 527.
- 2 GARLOCK, J. H. Gangrene of the finger following digital nerve block anesthesia. *Ann. Surg.*, 1931, 94, 1103.
- 3 HAUSER, E. D. W. Diseases of the Foot. Philadelphia and London: W. B. Saunders Co., 1939.
- 4 HIGGS, S. I. Hammer toe. *Med. Press & Circ.*, 1931, 131, 473.
- 5 JONES, R., and LOVETT, R. W. Orthopedic Surgery. New York: William Wood & Co., 1929.
- 6 LAKE, N. C. The Foot. Baltimore: William Wood & Co., 1935.
- 7 LAPIDUS, P. W. Operation for correction of hammer toe. *J. Bone & Joint Surg.*, 1930, 31, 977.
- 8 SELIG, S. Objections to the use of Kirschner wire for femoral neck fractures. *J. Bone & Joint Surg.*, 1939, 31, 182.
- 9 THIRRY, A. Hammer Toe, the Cup and Ball Procedure. *La Pratique Chirurgicale Illustrée*. Ed. Victor Pauchet, 2d ed., p. 265. Paris: G. Doin and Co., 1937.
- 10 TRETLOWAN, W. H. The treatment of hammer toe. *Lancet*, 1925, 1, 1257, 1312.
- 11 WALLITT. Multiple arthroplasties in restorative straightening of hammer toes. *Rev. de chir. stric-tive*, 1937, 7, 122.
- 12 YOUNG, C. S. An operation for the correction of hammer toe and claw toe. *J. Bone & Joint Surg.*, 1938, 20, 715.

# FRACTURES IN THE NECK OF THE FEMUR—ACCURATE SUBCUTANEOUS FIXATION WITH SCREWS

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THERE is no need to enumerate the many advantages of internal fixation for fracture in the neck of the femur, for such treatment has revolutionized the care of this difficult fracture and, as several of them have remarked, has come to stay. In January, 1939, the Report of the Fracture Committee of the American Academy of Orthopaedic Surgeons ( ) gave a detailed account of the results in 485 intracapsular fractures treated by 600 surgeons or their clinics. Union occurred in 89.4 per cent of these cases, and the mortality rate was only 8.5 per cent. Debility and advanced years are indications and not contra-indications for internal fixation, as this type of treatment immobilizes the fracture while the patient's strength is sustained and complications are avoided by activity. Only a short period of hospitalization is necessary and nursing is greatly facilitated.

A majority of surgeons, although realizing the value of this treatment, have experienced considerable trouble and in some instances have had trying ordeals with internal fixation operations. Even upon exposure of the femur and the use of various types of finders and directors with numerous x-ray examinations during the operation the procedure has, as a whole, been difficult and time-consuming. Many surgeons do not attempt internal fixation because they realize these technical difficulties.

## INTERNAL FIXATION WITH SCREWS

A number of authors have reported excellent results with two screws which permit firm fixation with coaptation of the fragments. The relative simplicity and security of this form of fixation first advocated by Martin and later by Brewster (2) and others, have been borne out by our experience with 50 cases. In order to shorten the procedure and to insure greater accuracy a method has been devised whereby instead of exposing the femur these two screws are inserted subcutaneously under anteroposterior visualization with the fluoroscope. The screws are driven in through a very small incision in the lateral aspect

of the thigh (4, 5). This simple instrument has proved to be satisfactory in the majority of cases.

Our main difficulty with this form of internal fixation is the lateral placement of the screws which cannot be visualized with the ordinary fluoroscope. We formerly placed entire dependence upon holding the limb rotated internally while inserting the screws in a horizontal direction. Reliance upon this position in various techniques of blind internal fixation explains the failures which have occurred in many cases. Quoting Smith-Petersen himself: "The nail now driven in. It is kept in the horizontal plane unless the lateral roentgenogram shows that the neck of the femur deviates from this plane. If it does, proper correction is made." This dependence upon internal rotation alone caused failure in several of our cases, as the screws did not cross the line of fracture and protruded outside the neck. The error in these cases was due to two factors which altered the plane of the neck as related to the plane of the table. First, there is difference in the degree of internal rotation to which every leg can be turned. The second and more important factor is a considerable anatomical variation in the angle at which the neck leaves the shaft as compared to the plane of the patella. Stenrodler states that according to Mikulicz the torsion of the neck of the femur on the shaft varies in wide limits, from -20 degrees (posterior twist) to +38 degrees (anterior twist). The anterior twist or anteversion is a common occurrence.

To overcome this difficulty of accurate insertion in the lateral plane, a steel pin and block devised by Dr. Alfred Tuttle have been added to the original instrument. The pin is thrust along the anterior aspect of the femoral neck, thus guiding the cannula exactly to the central axis in the lateral plane. Since the addition of this guide the screws have been placed accurately in every case. Advanced age and debility are not contra-indications for this type of fixation, as the technique is rapid and is not shocking and does not require exposure of the femur. The steel screws used are 3, 3½ and 4 inches in length and of 6, 8 and 10 gauge, the size being selected according to the length of the femoral neck. The heads of the

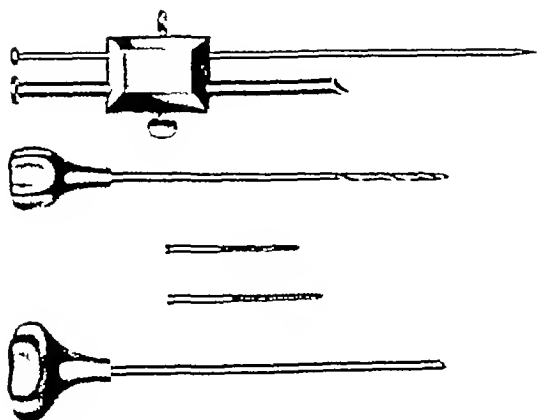


Fig. 1. Instruments for subcutaneous internal fixation. The cannula for insertion of the screws is parallel to and  $\frac{1}{8}$  inch from the pin which guides it to the central axis of the femoral neck. Screws of proper length are selected for the individual case.

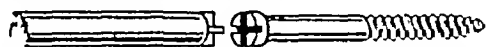


Fig. 11. Screw of stainless steel with a modified Phillips head and screw driver to fit.

screws are  $\frac{1}{4}$  inch in diameter and fit accurately in the cannula. Steel screws appear as satisfactory as several we had cast in vitallium, and appear to have caused foreign body reaction or absorption of the bone around them in only 1 case. We attribute the lack of bone absorption to the tightness of this form of fixation. Our observations have been in accordance with those of Brewster (5) who states that he never has found

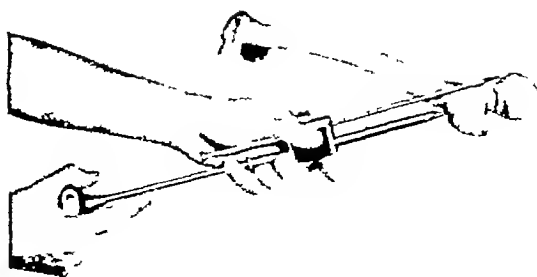


Fig. 2. Instrument assembled and placed on the femur. The guide pin is thrust along the anterior surface of the neck until it reaches the head of the femur. As this surface of the neck is nearly flat it can be followed easily. The cannula then is thrust through the soft structures until it reaches the lateral surface of the femur and being parallel to the pin the screws inserted through it will penetrate the central axis regardless of the angle of torsion in the neck.

it necessary to remove the screws from cases in which union occurred, and he has followed many individuals without any complaints or any evidence of absorption for a period of 10 years.

#### TECHNIQUE

Our choice of anesthesia is pentothal sodium administered intravenously. Ether and gaseous

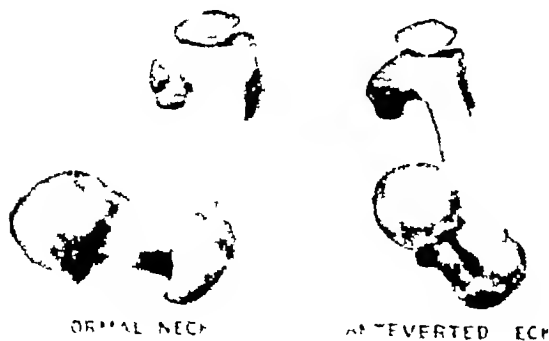
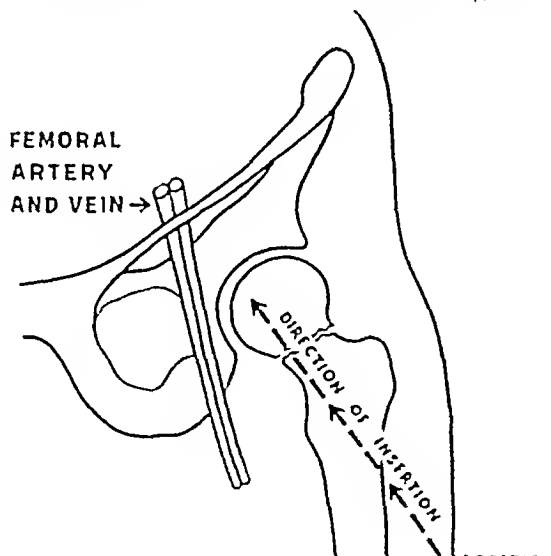




Fig. 3. General setup for subcutaneous operation. An assistant holds the limb in moderate internal rotation and abduction, and the knee of the other limb is flexed over the opposite side of the table. A small table with the special instruments, scalpel, and Michel clip is close to the operator. The fluoroscopic screen is over the hip.

agents are avoided on account of the use of the fluoroscope. In the treatment of intracapsular fractures, displacement of the fragments is reduced by the Leadbetter method and the final position is checked by anteroposterior and lateral roentgenograms. After complete reduction the affected limb is held in wide abduction and internal rotation; the knee of the opposite limb being flexed over the side of the fluoroscopic or fracture table. For this purpose orderlies serve better than doctors, as the latter become interested in watching the technique and may neglect to hold the limbs properly. The patient is protected from the roentgen rays by a 4 millimeter aluminum filter placed over the tube. The surgeon wears a lead-rubber apron, and his hands are absolutely protected by the use of a box covered with 1/4 inch sheet lead through which the entire operation is performed. The skin is painted and draped, only a small area distal to the greater trochanter being exposed. Then the room is darkened and the site of the incision, which should be on a line with the neck of the femur, is marked on the skin over the lateral surface of the hip. The lights are turned on and a 1 1/4 inch transverse incision through the skin and deep fascia is made, this point being at a considerable distance below the greater trochanter. The sterilized lead box is placed against the hip and the end of the instrument is introduced through the incision. Again the room is darkened and next the guide pin is thrust obliquely through the soft structures to the lateral aspect of the femur in a line with the femoral neck. Then keeping close to the neck or

surface of the neck of the femur, which is relatively flat, the pin is thrust further inward until it touches the head of the femur where it remains firmly fixed. By directing the pin along the neck of the femur under continuous fluoroscopic visualization there is no danger of injury to the femoral vessels, which lie 3/4 inches anterior and 3/4 inches inward in respect to the neck and head of the femur. The cannula is thrust through the soft tissues, and being parallel to the pin, which rests upon the anterior surface of the femoral neck, it points directly to its central axis. The instrument will be in the correct plane regardless of whatever torsion there may be in the neck of any femur. Next, with the aid of the fluoroscope the drill is inserted through the cannula, and a hole is bored obliquely upward through the outer fragment in a line with the neck. The operator may select the proper length of screws by holding one over the head and neck of the femur under the fluoroscope. It is better to use screws a little too long than too short. A screw is placed in the cannula and is driven across the neck with the special screw driver, the depth and direction of the screw being checked by the intermittent use of the fluoroscope. Then the guide pin is partially withdrawn and is replaced 1/2 or 3/4 inch above the first location and parallel to it on the neck of the femur, and the second screw is inserted through the accompanying cannula in a similar manner. Finally the hip is roentgenographed in both the anteroposterior and lateral planes in order to check the exact position of the screws. If the screws are placed a little too



Fig 6 Lead covered box for protection of the operator's hands. The instruments are manipulated through the slot. A rectangular piece of lead rubber clipped to the side of the hip may be used instead of the lead box

deep or not quite deep enough, they may be adjusted at this time. The instrument now is withdrawn, and the skin incision is closed with two or three Michel clips. This method requires an average time of 23 minutes.

#### POSTOPERATIVE CARE

No shock and very little pain follow this procedure. Neither splinting nor traction is used. Careful attention is given to the patient's general condition and immediate function is encouraged. Occasionally the surgeon must move the hip and knee in order to convince the patient that he has control of it, and then frequent exercises are ordered. In most instances the patient is helped to sit over the side of the bed on the first day after operation, although in debilitated individuals it has been found best to wait and only use a back-rest for a few days. After confidence has been restored by turning and sitting on the side of the bed the patient is further encouraged to slide over the side of the bed and to stand beside it without aid, touching only the foot of the affected limb to the floor. After thus learning to balance properly the use of crutches is relatively easy. It is not advisable under any circumstances to stand the patient up on crutches without these preliminaries. The use of a wheel chair is avoided, as this promotes inactivity. Weight bearing without crutches is not permitted until periodic x-ray examination shows union. It should be remembered that fractures occurring in the femur always unite endosteally without any evidence being shown of external callus and that bone tribulation is the only definite proof the union has been accomplished.

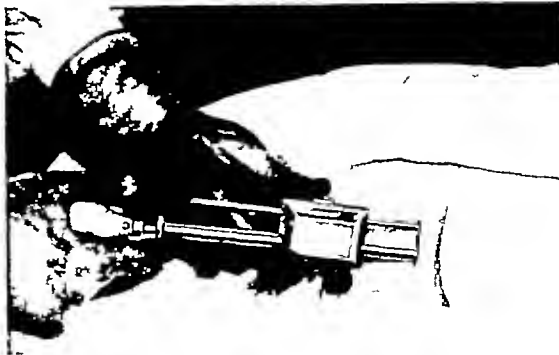


Fig 7 The guide pin has been inserted over the anterior surface of the femoral neck and a hole is being drilled through the outer fragment. The lead covered box is omitted for the photograph.

#### RESULTS

There were 50 cases in this series. The average age was 73 years. The average hospitalization period was 24 days. The average time required for operation was 23 minutes. Operative infection occurred in no case. There were no operative deaths. There were 3 operative failures.<sup>1</sup> Reoperation (re-insertion of screws)<sup>2</sup> was necessary in 2 cases. Screws were removed<sup>3</sup> in 2 cases.

<sup>1</sup>In one case the screw were too short to reach the subcapital fragment. In another case there evidently was a decided anteversion of the neck and the operator failed to insert the screws across the fragments. In the third case in which there was non union and displacement for 15 months after the injury the fragment could not be reduced by manipulation. An attempt to hold the fracture by inserting the screws in various directions failed.

<sup>2</sup>Reinsertion was successful.

<sup>3</sup>In 1 case there was a small area of absorption of the bone around the screws although at operation 15 months after the internal fixation there was firm union without deformity. In the other case there was persistent pain operation was permitted only for removal of screw.

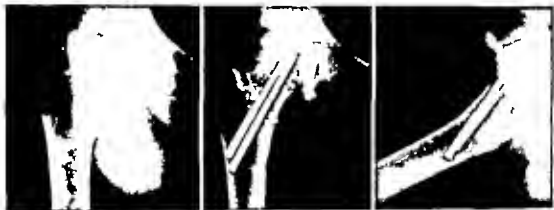


Fig 8 The wound is closed with 2 or 3 Michel clips.



b

Fig 9. Transcervical fracture. a, Before treatment. b, anteroposterior film after fixation. c, lateral view.



b

Fig 10. Transcervical fracture. a, Before treatment. b, anteroposterior film after fixation. c, lateral view.



Fig 11. Fracture at the base of the neck.

re film after fixation lateral view

Non-union<sup>1</sup> occurred in no case. The first patient was operated upon in October, 1936. Union has occurred in all of the cases which have been followed, except those which were ununited when the screws were inserted. Several debilitated patients died within a few weeks after operation and before discharge, but not as the result of the operation. A number of the entire series died a few months later on account of heart failure, diabetes, dementia, and embolism.

#### SUMMARY

An accurate technique of internal fixation which is satisfactory for all fractures in the neck of the femur has been described. It is safe and requires only a short time. The steel screws used have not caused foreign body reaction, and are inexpensive. Our experience with this method has proved its value.

<sup>1</sup>In 1 of these cases non-union had been present 6 months and in another for 15 months before these operations were performed. The procedure was of no benefit in either case.

The instrument described was perfected with the cooperation of George P. Pilling and Son Company, Philadelphia.

#### BIBLIOGRAPHY

- 1 Treatment of fractures of the neck of the femur by internal fixation. Report of the Fracture Committee of the American Academy of Orthopaedic Surgeons. *J. Bone & Joint Surg.*, 1939, 21: 483.
- 2 BREWSTER, W. R. Fractures of the upper extremity of the femur neck and trochanters. *Am. J. Surg.*, 1938, 42: 662.
- 3 BREWSTER, W. R. Personal communication.
- 4 GECKELER, E. O. Subcutaneous fixation with screws for fractures of the hip joint. *Am. J. Surg.*, 1937, 37: 396.
- 5 Idem. The problem of the unsolved fracture. *Hahnemann Month.*, 1936, 71: 905.
- 6 MARTIN, E. D. Fractures of the neck of the femur. *Internat. J. Med. & Surg.*, 1933, 46: 30.
- 7 SMITH-PETERSEN, M. N. Treatment of fractures of the neck of the femur by internal fixation. *Surg., Gynec. & Obst.*, 1937, 64: 287.
- 8 STEINDLER, A. *Mechanics of Normal and Pathological Locomotion in Man*. Springfield, Illinois: Charles C. Thomas, 1935.



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### URETERO-INTESTINAL ANASTOMOSIS AND CYSTECTOMY

**T**RANSPLANTATION of the ureters into the sigmoid with cystectomy has been established as a sound surgical procedure in recent years. Before the introduction of intravenous urography the general opinion was that dilatation of the ureters and consequent renal sepsis invariably occurred following this operation. These deductions were based upon a very small number of cases in which examination was made after death from liverne causes and at varying interval after the operation and they have been proved unwarranted by more extensive investigations. By modern roentgenographic technique it can be demonstrated that the ureters and kidneys remain normal or nearly so for a period of years, when the operation has been performed with proper care.

Ureterosigmoidal anastomosis is accepted as the procedure of choice for the relief of extrophy of the bladder in children but there is some difference of opinion among surgeons

as to the age at which the operation should be performed. In the past, the consensus was that the operation should be postponed until the child was four or five years of age despite the fact, established by numerous observers, that the ureters may become dilated and the child may succumb to renal sepsis before this age is attained. In the last two or three years it has been demonstrated that the ureters may be implanted into the bowel of infants less than one year of age with a surprisingly low mortality and with satisfactory end-results. The procedure has been tolerated well, and it has been accomplished without complications from renal infection because in very young children the bacteria in the intestines are less virulent and less abundant than in older children.

In a few children with epispadias the surgical defect is so extensive that the sphincters are involved and even though the continuity of the urethra is established incontinence persists. If plastic operations fail to correct the incontinence diversion of the urine into the bowel is justifiable to eliminate the constant soiling of the clothing with urine and to make the patient comfortable.

The majority of women with vesicovaginal fistula may be cured by plastic procedures, but occasionally operations of this type are contra-indicated because of the extent of the defect, or because of replacement of normal tissue by scar tissue following unsuccessful surgical treatment previously. In carefully selected cases of this type ureterosigmoidal transplantation affords complete relief.

In some instances when nephrectomy is performed for renal tuberculosis and in rare cases of Hunner ulcer the patient fails to

respond to conservative therapeutic measures, and suffers intolerable pain, accompanied by diurnal and nocturnal frequency, and pronounced dysuria. These symptoms may be completely relieved by diversion of the urinary stream into the bowel, leaving the bladder intact.

The value of cystectomy and transplantation of the ureters into the bowel in selected cases of carcinoma of the bladder has been the subject of considerable discussion and controversy in recent years. While there is but little doubt that complete cystectomy is the preferred operation in the management of certain cases of vesical carcinoma, the indications for the operation are still debatable. In the past, this operation was advocated only when extensive invasion of the bladder had taken place, with considerable dilatation of the ureters. The transplantation of such ureters is bound to be accompanied by a high rate of mortality. Hence the procedure of choice in this type of case is cutaneous ureterostomy and cystectomy.

There is a group of cases of carcinoma, however, in which cystectomy and transplantation of the ureters should receive serious attention. When the new-growth is situated at the base of the bladder and the ureteral orifices are encroached upon or the vesical sphincter is invaded, when extensive multiple or single infiltrating tumors are present, or when multiple recurring tumors develop rapidly and cannot be controlled by fulguration, the radical operation should be considered. Before advising this operation, however, certain other factors must be carefully appraised. Renal function must be adequate, preferably in both kidneys, at least it must be approximately normal in one kidney. Intravenous urography should demonstrate that the caliber of the ureters is such that their transplantation into the bowel is technically feasible.

There should be no evidence of acute or sub-acute pyelonephritis. A biopsy should be secured to determine the degree of malignancy of the lesion before the cystectomy is performed. If there is evidence of metastasis or extension of the tumor beyond the confines of the bladder, there is no possibility of a cure, and the patient should not be subjected to the radical procedure.

No phase of the treatment is more important than the preparation of the patient before operation. As a general rule, four to six days are required to cleanse the bowel, to improve renal function, and to control renal infection.

Numerous individual operative techniques have been presented in the literature. As a rule, however, the original submucous technique of implanting the ureter into the bowel, or one of a number of modifications, is employed. Simplicity is the criterion of any satisfactory operation, the more complicated the procedure, the higher the operative mortality. In addition, the operative technique should include rigid attention to asepsis, lack of tension at the site of the anastomosis, absence of obstruction and kinking of the ureter, and immobilization of the bowel. The decision as to whether unilateral or simultaneous bilateral transplantation should be performed is influenced by the general condition of the patient, the caliber of the ureters, the condition of renal function, and the presence or absence of renal infection, as well as the personal experience of the surgeon. Although in many instances unilateral transplantation of the ureter is advisable, bilateral transplantation in well selected cases can be performed with equally successful results.

When the unilateral procedure is chosen, the operation may be performed in two or three stages, that is, by transplanting the ureters singly, and finally removing the bladder, or by

performing the cystectomy at the time the second ureter is transplanted into the bowel. If simultaneous transplantation is performed the bladder may be removed two weeks later. When the transfixion suture technique is employed both ureters may be transplanted simultaneously as there is no interruption in the urinary stream to the bladder until after the new channel into the bowel has been established.

When the cases are wisely selected and the technique carefully carried out, ureterosigmoidal anastomosis is a valuable and at times, a life-saving measure. The patient is comfortable, the rectum serves well as a reservoir for the urine, and a natural sphincter under voluntary control, eliminates soiling of the clothing. He is able to resume normal life and activities and even to return to a gainful occupation. It cannot be stressed too strongly that the results to be obtained from ureterosigmoidal transplantation depend, perhaps more than in any other field of surgery, upon the individualization and proper selection of cases.

CHARLES C. HROODIN

## CLINICAL INVESTIGATION

A RECENT editorial in one of our most widely read journals called attention to the importance of clinical investigation. Harvey Cushing in his address before the Seventeenth International Congress of Medicine in London in 1913 said: "Nature is loath to give up her secrets; discoveries do not come by chance; they are made by those only who are industriously prepared to observe them. He realized that clinical investigation was important for he once said: 'Let us not forget that investigation at the bedside is just as important as investigation in the purely experimental workshop.' Cushing's concept of clinical investigation was work

carefully planned rigidly controlled, and skillfully executed, free from bias and statistically sound. Good clinical investigation is often far more difficult than animal investigation and much of it is an extension of work begun in a laboratory of the fundamental sciences.

Clinical investigation should wherever possible be done under conditions which permit of the most rigid type of control and much of it should be done by men who have had some preparation in the field of investigation. I find myself in agreement with Cutler who in speaking of training in a good experimental laboratory found that this involves training in "accurate observations, logical deduction and the bringing forth of conclusions based on fact. It tends to do away with conjecture, ideas based on supposition, hearsay and single isolated observations." The statement that

the physician cannot always wait until the fundamental discoveries have been established beyond a shadow of doubt in the laboratory is beyond question, but the physician can wait until he has proof beyond reasonable doubt on the basis of carefully made clinical experiments, before publication of his clinical observations. Hasty publication based on too few data, or on data not carefully compiled and studied, has resulted in the temporary wide spread adoption of many methods of therapy which were finally proved to be worthless.

There is now general agreement that surgical competence is hardly to be considered in the widely divergent data on mortality of operations for perforated ulcer, the acutely inflamed gall bladder, and acute appendicitis with peritonitis. Elliott Cutler once said, "The explanations for our surgical failures are to be found in the bacteriological and physiological laboratories more frequently than in the anatomical rooms."

If Roscoe Graham is correct, and I believe he is, that, in the treatment of perforation of a

gastric or duodenal ulcer, the surgeon's sole function is to save life, Junghanns cannot be correct when he advocates subtotal resection of the stomach in the presence of a grossly contaminated peritoneum. Recent controversial articles upon whether the acute inflamed gall bladder should be treated by "skilful neglect," immediate cholecystostomy or immediate cholecystectomy, frequently fail to point out the changing pathologic characteristics of the process over a period of hours, a factor that should cause the operator to vary the procedure depending upon what is exposed during the operation. The statement frequently made that the acutely inflamed gall bladder should be treated like the acutely inflamed appendix demonstrates a lack of consideration of the sequelæ of these two processes. The apparent widespread disparity in mortality in good surgical clinics following operations for acute appendicitis associated with peritonitis cannot be due entirely to differences in the incision, anesthesia, and other factors under control of the surgeon. In very few of the papers that have been published are the data on the extent of the peritonitis of real sig-

nificance. The use of the term "generalized peritonitis" in clinical writing should be condemned. This is an autopsy diagnosis and the surgeon who attempts to determine the extent of the infection during the operation is playing with the life of the patient. Some surgeons record the patient as having peritonitis only when a positive culture is obtained from the fluid present in the peritoneal cavity at operation, and others when a turbid fluid, which consists almost entirely of leucocytes and histiocytes, is present.

Laboratory investigation which has been carefully planned and carefully executed can be repeated by the same methods, by the same controls, in the same or other laboratories. We have a right to demand similar criteria for clinical investigation. There is no need to separate the clinician and the investigator. There is every reason to bring them together. In this sense every well qualified practitioner should be inquisitive and if he is, he will find much to observe and investigate. If he develops the scientific method of accurate observation, he will correlate his findings and be more likely to draw sound deductions.

I S RAVDIN

# TEXTS AND DOCUMENTS

## REPORT OF THE AUTOPSY OF THE SIAMESE TWINS TOGETHER WITH OTHER INTERESTING INFORMATION COVERING THEIR LIFE<sup>1</sup>

A Sketch of the Life of Chang and Eng

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THOUGH many of us refer rather glibly to the original Siamese twins, few of us are old enough to recall the time when these two gentlemen created a medical and public sensation in this country some 67 years ago. It is, furthermore, fair to state that few pathologists, here or abroad, are or ever have been familiar with the interesting necropsy report on these twins by very capable men, and certain aspects of their life in conjunction with the autopsy findings have a particularly important bearing on the interpretation of data collected by those physiologists and experimental pathologists who by surgical methods attempt to produce experimental parabolic twins in studies of avitaminoses or endocrinology for although the original Siamese twins had a common liver the parenchymatous tissue being seemingly continuous between them,

the one twin, Eng, was not affected when the other Chang was intoxicated, which was rather frequent neither did the sickness of one ever affect the other nor did the bilious attacks common to both affect the brothers simultaneously. Most of this would seem to indicate "that there was no free interchange in their circulation. The probability that the twins arose from a single ovum raises a theological question as to whether the twins had one or two souls, etc., since according to some theologies a single soul is implanted at the time of conception. This same question, of course, can be raised in connection with the souls of all identical twins. The sociological aspects of the life of such twins will occur naturally to the reader.

The text of the report published in 1874 now follows —

IN the present article it is not purposed to give an elaborate history of these famous twins, but only to put on record certain well-ascertained facts of physiological interest in regard to their life, to give all that can be ascertained as to the circumstances of their death, and to offer a brief history of the manner in which their bodies were brought to Philadelphia.

According to a writer in *Lippincott's Magazine* for March, the Siamese Twins were born in 1811 some thirty miles southwest of Bangkok their father being a Chinaman, their mother a native of Siam, bred by a Chinese father. The twins were therefore, three fourths Chinese, and were known in their native home as the 'Chang and Eng' Twins. They were the first-born sons of their parents but their mother has presented her husband with four

other pairs of twins and four children born at single births—all of them normal and healthy. Their mother during their infancy entirely recognized their separate individuality and also the fact that there existed a common sensibility in the centre of the band. She stated, what is undoubtedly true, that at first the ligament was so short that the boys were compelled always to be face to face even in the bed they could not turn without being lifted up and placed in the desired position. As they grew the ligament seemed gradually to stretch, until they were able to stand side by side, and even back to back, and to turn themselves in bed by rolling one over the other. The father being a fisherman of the laboring class, the boys lived in one of the floating houses of the country and soon became famous swimmers, spending much of their time in the river. It was the peculiarity of their movements in the water

<sup>1</sup> Reported from the Philadelphia Medical Times. Philadelphia: J. B. Lippincott & Co. Also given with illustrations.

which first attracted the attention of a Scotch merchant, Mr Robert Hunter, and finally led to their leaving their native country in quest of fortune

For many years Chang and Eng Bunker lived in North Carolina, where they were married, and raised large families of children, Chang being the father of ten, Eng of nine Dr Joseph Hollingsworth, to whom we are indebted for the information given in this article as to their habits of life and the circumstances of their death, states that he had known them as residents in the neighborhood of Mount Airy, North Carolina, for some twenty years, during which time he had acted as their family physician Chang, who is said to have derived his name from the Siamese word for "left," was the left of the pair, and was much smaller and more feeble than his brother Eng, whose name signifies "right." Their habits were very active during the latter part of their life they and their families lived in two houses, about a mile and a half apart, and it was an inflexible rule that they should pass three days alternately at each house So determinedly was this alternation maintained that sickness and death in one family had no effect upon the movements of the father, and a dying or dead child was on one occasion left in obedience to it indeed, Dr Hollingsworth is very positively of the opinion that the death of the twins themselves was the result of this rule, or, at least, was materially hastened thereby This will be made apparent hereafter

The evidences during life that the twins were physiologically distinct entities were very numerous and apparent. They were different in form, tastes, and disposition, all their physical functions were performed separately and unconnectedly What Chang liked to eat, Eng detested Eng was very good-natured, Chang cross and irritable The sickness of one had no effect upon the other, so that while one would be suffering from fever the pulse of the other would beat at its natural rate The twins not rarely suffered from bilious attacks, but one never suffered at the same time as the other, a circumstance which seems somewhat singular in view of the close connection which the postmortem has shown to exist between the livers of the pair Chang drank pretty heavily—at times getting drunk, but Eng never felt any influence from the debauch of his brother—a seemingly conclusive proof that there was no free interchange in their circulations

The twins often quarrelled, and of course, under the circumstances, their quarrels were bitter They sometimes came to blows, and on one occasion came under the jurisdiction of the

courts After one of these difficulties Chang and Eng applied to Dr Hollingsworth to separate them, stating that they could not live longer together Eng affirmed that Chang was so bad that he could live no longer with him, and Chang stated that he was satisfied to be separated, only asking that he be given an equal chance with his brother, and that the band be cut exactly in the middle But as Dr Hollingsworth advised very decidedly against this, and declined to interfere, cooler counsels prevailed upon the twins to remain as they were

In August, 1870, Chang suffered from a paralytic stroke, from which he never fully recovered, and during the last year of his life he several times said to Dr Hollingsworth, "We can't live long "

On the Thursday evening preceding their death, the time having arrived for their departure from the house at which they were staying, the twins rode a mile and a half in an open wagon The weather was very cold—the night being the severest of the winter Chang had been complaining for some days of cough, with distress and actual pain in the chest He was so unwell that his wife thought he would be unable to bear the trip, but he finally went On Friday morning Chang reported that he felt better, but that in the night he had had such severe pain in the chest, and so much distress, that he thought he should have died

The twins slept in a room by themselves or with only a very young child present, and some time in the course of Friday night they got up and sat by the fire As they were accustomed to do this frequently, nothing was thought of it by those of the family who saw them, even though they heard Eng saying he was sleepy and wanted to retire, and Chang insisting on remaining up, stating that his breathing was so bad that it would kill him to lie down Finally, however, the couple went to bed again, and after an hour or so the family heard someone call No one went to the twins for some time, and, when they did go, Chang was dead, and Eng was awake He told his wife that he was very "bad off" and could not live He complained of agonizing pain and distress especially in his limbs His surface was covered with a cold sweat At his request his wife and children rubbed his legs and arms, and pulled and stretched them forcibly This was steadily continued until he went into a stupor, which took place about an hour after the family were alarmed The stupor continued up to death according to the statements of the family, there were no convulsions

Dr Hollingsworth did not reach the house until after the death of both of the twins. He found the wives, and especially the children, averse to any postmortem being made, but, after much persuasion obtained permission to put the bodies in a position to be preserved until he could obtain someone from Philadelphia to perform the autopsy. He placed the bodies, after they had been thoroughly cooled, in a coffin, which was put in a wooden box, which was, in its turn, enclosed in tin the whole being buried in a dry cellar in such a way as to be imbedded in charcoal.

As bearing upon the question, What was the cause of the death of Chang? it is important to state that Dr Hollingsworth had repeatedly told Chang and Eng that, in his opinion, the death of one did not necessarily compromise the life of the other that he could separate them, by cutting close to the body of the dead one, without killing the living one. It would appear possible, in view of this, that the death of Eng was not simply the result of fright.

Shortly after the death of the Siamese Twins, Dr William Pancoast requested the Mayor of Philadelphia to telegraph to the Mayor of Greensboro North Carolina, in regard to the possibility of a postmortem examination being obtained. To this the Mayor of Greensboro substantially replied that he had neither knowledge nor power in the matter. When Dr Hollingsworth, *en route* North, arrived at Greensboro the telegram of Dr Pancoast was handed to him. On the evening of his arrival at Philadelphia (Friday) he saw Dr Pancoast and Prof Gross, and a letter was written to the wives of the twins, proposing that Dr Pancoast should come on to embalm and examine the bodies.

On Sunday Dr Hollingsworth saw Prof. John Neill and, on consultation, it was concluded that the matter was of public importance, and should not be confined to any single private individual. As the promptest method, it was deemed best to call a meeting of such physicians as were interested in the matter and could be hastily got together.

The meeting took place on the evening of Monday January 26 1874 at the house of Dr Neill but, although a number had been asked, only Prof Leidy and Dr Ruschenberger besides Drs. Hollingsworth and Neill, were present at the conference. As the result of their deliberations, it was determined that two gentlemen should be at once dispatched to the home of the twins, in order to examine and embalm the bodies as speedily as possible and it was agreed that Drs. William H

Pancoast and Harrison Allen should be requested to go.

It will be seen at once that the College of Physicians was in no wise responsible for the acts of the Commission although its name was freely used by the prominent Fellows engaged in the transaction. Indeed, these gentlemen, recognizing this, were prepared to meet the expenses of the trip had the College failed to endorse their action.

Owing to various obstacles and embarrassments, the Commission did not leave the city until Thursday night, January 29. At the request of Dr Pancoast, Dr Andrews went with the party as a companion and aid.

The Commission arrived at Mt. Airy on the evening of Saturday January 31 and proceeded to the residence of Eng the following morning, in company with a photographer and Dr William Hollingsworth, who is the family physician in the absence of Dr Joseph Hollingsworth. The widows of the twins received the Commission hospitably and a conference was at once entered into, at which the "Mistresses Bunker the Commission, Dr Hollingsworth, and the widows' legal adviser were present. It was then agreed that, under consideration of embalming the bodies of the twins, permission would be granted to exhume and examine the structures distinguishing them, provided that no incision should be made which would impair the external surface of the band. Subsequently it was agreed that limited incisions would be allowed on the posterior surface of the band. An agreement in writing was then drawn up expressing the above restrictions, but extending the authority to the Commission to remove the bodies to Philadelphia, provided that they be kept in a fireproof building and held subject to the commands of the families when informed of the completion of the embalming process.

The object of the visit of the Commission, having been noted about the country had attracted a crowd of curious people, who were willing enough to give the necessary aid in exhuming the bodies. The circumstances attending this were briefly as follows. The bodies were buried in the cellar of Eng's house, in a shallow grave, which had been covered with a tumulus of powdered charcoal. This being removed revealed several planks covering an outer wooden box, which, in turn, enclosed a tin encasement to the coffin. After unscrewing the tin box, the coffin was unscrewed and the object of the search was exposed to view. It was certainly a low moment. Fifteen days had elapsed since death, and no preservative had been employed. It was an agreeable surprise, therefore, that no odor of

decomposition escaped into the room, and that the features gave no evidence of impending decay. On the contrary, the face of Eng was that of one sleeping, and the only unfavorable appearance in Chang was a slight lividity of the lips and a purplish discoloration about the ears. The widows at this point entered the room, and, amid the respectful silence of all present, took a last look at the remains.

The room was then cleared of all not connected with the work of the Commission, the bodies were disrobed, and preparations at once begun to secure photographs. The bodies were held in an erect position, and negatives of the entire figures, and views of the band at short foci, were secured. The day being cloudy, much time was necessarily expended in obtaining these pictures—time sufficient for a number of observations upon the external appearance of the bodies to be recorded. The notes are given just as they were taken at the time.

*Examination made Sunday, February 1, 1874, fifteen days and eight hours after the death of Chang*

The bodies were found in the coffin in a good state of preservation, there was a slight cadaveric odor about Chang, with marked passive congestion of the back of the arms and neck on both sides, and in a less degree of the posterior aspect of the forearms, buttocks, thighs, and legs, there was none on the feet, where, however, there was marked fulness of the superficial veins, this was better marked on the left side. There was a greenish discoloration on the anterior abdominal wall.

*Face*—Lips moist and discolored, peculiar reddish congestion sparsely distributed over malar prominence and beneath ear. The thoracic discoloration was much deeper on the side next to Eng.

The left nipple was visible in front well towards the middle line, the right one just showing. The fingers of the right hand—the paralyzed side—were forcibly flexed, although *rigor mortis* was absent.

In Eng there was passive congestion of back, most marked on buttocks and infra-spinous spaces—none on the front of the body, slight greenish discoloration of anterior abdominal wall.

In both subjects the hair of the head was gray.

On the *pubis* of each subject the hair of the *left side* was gray, that of the *right side*, black.

The process of embalming was now begun. Incisions were made to the outer side of the median line of the abdomen in each individual, extending from the inferior margin of the thorax to a point midway between the symphysis pubis and the

anterior spinous process of the ilium. The aorta was reached after the usual method, but was found to be in an atheromatous condition, compelling the selection of the left primitive iliac for the insertion of the pipe. A solution of chloride of zinc was then injected.

After the embalment had been completed, the incision was continued upward and inward towards the band. Examination of the band through this incision convinced the Commission of the complex nature of the band, and suggested the suspension of a complete study of the parts until removal of the bodies to Philadelphia. The fact that the photographs had been far from satisfactory strengthened the Commission in its decision to stop the investigation at this stage. The incisions were, therefore, sewn up, the clothing readjusted, and the bodies placed in the coffin and conveyed to Mt Airy. Here the tin box which was used for the temporary burial was again brought into use, and the lid carefully resoldered. Without delay the Commission started on its return to Philadelphia, expressing the bodies at Salem.

The Commission arrived in Philadelphia, February 5, having been absent one week.

Upon the arrival of the bodies at the College of Physicians, they were placed in the care of the committee upon the Mütter Museum and of the Hall Committee, and were closely locked and guarded until a special meeting of the College was called, upon Monday evening, February 8, when, after considerable discussion, it was agreed that the College should accept the action of its Fellows and pay the expenses of the trip. Further, a vote of thanks was given to the gentlemen who went to North Carolina, and to Dr Hollingsworth, and the Mütter Committee was authorized to appropriate three hundred and fifty dollars for the preparation of casts and photographs, which should remain the property of the Museum. Finally, the College appointed the Mütter Museum Committee and the original Commission (Drs Pancoast and Allen) as a joint committee for carrying out the examination of the Siamese Twins, it being understood that a report and a demonstration of the specimens were to be made to a subsequent meeting of the College, also, that the dissections and the report were to be the work of the original Commission.

On Tuesday, the 10th instant, they were exposed for study. They were at that time found in a satisfactory condition, except the right lower extremity of Chang, which required immediate care to prevent further destructive changes taking place.



## STATEMENT

*Statement of Eng's widow made to the Commission at Mount Airy*—The paralytic stroke from which Chang had suffered occurred about three years ago when he was at sea, seven days out from Liverpool. He had been intemperate for some time previously and had been drinking hard on board the vessel, being frequently intoxicated. He had never had mania à potu. Even when he was drunk, Eng was not affected. Two of his children had died one from phthisis, the other apparently from apoplexy. Eng had lost five children one each from phthisis, diphtheria, and dysentery one from the effects of a burn, and one still-born.

Chang died Saturday January 17. He had had a cough since the preceding Monday night. It was dry with scanty frothy sputum and no pain. Left lung probably involved, slight dullness on corresponding side. On Thursday January 15 his skin was acting freely and for that reason Dr Hollingsworth ordered him not to venture out, but in spite of that prohibition, he went as usual to Eng's. At the time of his arrival he had little cough and no expectoration, but loud bronchial rales were plainly heard by those around him.

When Eng saw his wife after learning that Chang was dead, he said, "I am dying but did not speak of his brother's death. He soon afterwards expressed a desire to defecate, and this continued for half an hour. He rubbed his upper extremities, raised them restlessly and complained of a choking sensation. The only notice he took of Chang was to move him nearer. His last words were, "May the Lord have mercy on my soul!"

### PHOTOGRAPHIC REPORT— THE SIAMESE TWINS AT THE COLLEGE OF PHYSICIANS

A special meeting of the College of Physicians of Philadelphia was held at the hall, Wednesday evening, February 18, for the purpose of hearing the report of the Commission on the Siamese Twins.—Dr W. S. W. Ruschenberger, U.S.N. in the chair. On the motion of Dr Gross, it was, after some discussion, resolved that the *Philadelphia Medical Times* be allowed to report the proceedings of the meeting on condition that three hundred copies of the journal should be given to the college for the use of the members.

The bodies of the Siamese Twins being upon the table the meeting proceeded to hear the report of Drs. Pancoast and Allen. On behalf of the Commission, Dr. Pancoast stated that, the dis-

section not having been entirely completed, their report would be a verbal one, to be followed at some later date by a memoir upon the subject. He further remarked that it had been agreed that he should consider chiefly the surgical aspect of the matter in hand, whilst to his colleague had been assigned the demonstration of the anatomical peculiarities.

## DR. WILLIAM H. PANCOAST.

*Mr. Chairman, and Fellows of the College*—Having been requested, as a member of the Commission, to open the discussion this evening, I will say briefly, in reference to this monster of symmetrical duplex development, joined, as many of the Fellows now know at the coniform appendix and also here at the oesophagus or navel, that at the investigation which we made on the first occasion at Mount Airy I made the opening incision of the body on the line for the hepatic of the primitive Blast, on the right side. Dr. Allen made the incision on the left. The object, as to reach the great vessels, the aorta and the two primitive iliacs, and to force the injecting material high and for embolizing (chloride of zinc) up the aorta and down the iliacs until it ran from the incisions made in the fingers and toes. It flowed freely through the blood vessels in Eng, owing to the ossified condition of his arteries; the injection in Chang, as, however, not so successful, owing to decomposition in the tissues and blood-vessels. It was necessary to repeat the injecting process several times in order to preserve the body. The arteries of Chang were found to be very much decomposed,—quite rotten, in fact.

I Thompson's *Medical Dictionary* we find the scientific name given for the Siamese Twins, in the classification of teratology to be *Xiphopagus* and by referring to the admirable article on *Diplozoology* of Dr. G. J. Fisher (published in the *Transactions of the Medical Society of the State of New York* for the year 1865), it will be found that the twins belong in the class of *Amacaulidymos*. In his classification of double monsters he makes three orders: *Order first*,—*Terminacaulidymos* derived from *teris*, *teris*, "acaulis," *hala*, "down," and *dialamos*, "twins." *Definition*,—duplicity with more or less separation, of the cerebral-apical axis, from above downwards. *Order second*,—*Terminacaulidymos*, derived from *teris*, "up" or "above," and *dialamos*, "twins." *Definition*,—duplicity with more or less separation, of the cerebral-apical axis, from below upwards, or from the caudal towards the cephalic extremity of the neural axis. *Order third*,—*Terminacaulidymos*, derived from *teris*, "above," *hala*, "down," and *dialamos*, "twins." *Definition*,—duplicity with more or less separation, of both the cephalic and the caudal extremity of the cerebral-apical axis, existing contemporaneously. In this order the monster now before us might be called an *Amacaulidymos*.

Thus we have the scientific nomenclature of this monster. Of course, the consideration of the greatest interest to the profession, and one of the main reasons why the Commission made such exertions to obtain this post-mortem, was that the American profession might not be charged with having neglected an effort to obtain an autopsy which could solve the mystery of their union. The nature of greatest interest is connected with this band,—about four inches long and eight inches in circumference. In addition to this, there are other points of importance in teratology in regard to the fulfillment of the law of homologous organs, in relation to the junction of the recti muscles and the fascia of the oblique and transverse at their point of meeting in the centre of the band in regard to the position

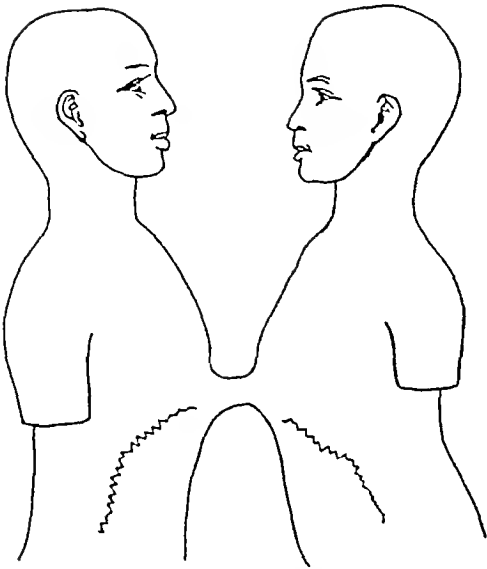


Fig 1 Diagram from a cast showing the position of the ligament and of the primary anterior incisions. During life the twins never assumed the face to-face position in which they are here represented and which is without doubt that of their foetal life

of the hearts, we think their apices present towards each other [This has since been found to be the case] The livers we have found to approximate to each other and to push through the respective peritoneal openings into the band. We extended our incisions to the margin of the band in front. By placing my hand in the peritoneal cavity of Eng and my colleague placing his hand in the peritoneal cavity of Chang, we pushed before us processes of peritoneum, which ran on to the median line of the band, and we could feel our fingers in the lower portion of the hand, behind the median line, with a distinct layer of peritoneum between them, demonstrating at once the prolongation of the peritoneum into the hand, and the complete separation of one peritoneal cavity from the other at this median line. Above that we felt some traces of vascular connection, apparently running from one liver to the other, but this we will examine into when we have a better opportunity of carefully dissecting and examining what vascular structures may exist. We also noticed that in turning off the flaps consisting of the anterior walls of the abdomen, the hypogastric arteries, as illustrated by the diagram on the blackboard, ran upwards in each body into the band. We lost them in this way, as we think, towards the common umbilicus in the anterior inferior surface of the middle of the band.

It is probable that the two hypogastric arteries on each side passed through this umbilicus. Whether or not there were two umbilical veins, we have not yet been able to decide, nor to answer the question whether the umbilical cord was double or single and composed of the four hypogastric arteries and two umbilical veins, or whether the placenta was single, double, or twin.

We also recognized that the ensiform appendix, as shown in the diagram of each side, was prolonged and united in the middle line. On our later examination, we find that there is complete continuity of structure of the cartilages,

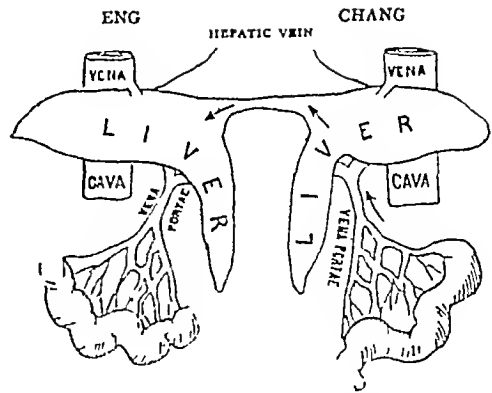


Fig 2 Diagrammatic representation of the livers, portraying the relations of the vessels, etc. The arrows show the directions in which the injection passed from Chang to Eng

but no true joint at the middle line, although it is possible there may be some small synovial sacs farther up. The motion is mainly due, as I here demonstrate to you by moving these bodies one upon the other, to the elasticity of the connected ensiform appendices and intervening fibro-cartilages.

In regard to the vascular connection of the band, we have not yet been able to make so thorough and careful an examination as we wished, but still, in throwing colored plaster into the portal circulation of Chang it has been found to flow through the vessels of the upper part of the band into the portal vessels of Eng. So that the surgical anatomy of the band consists in the skin and fascia which cover it, the two separate peritoneal pouches which meet in the middle, the large peritoneal pouch, the vascular connection, to whatever extent that may exist between the two portal circulations, and the remains of the hypogastric arteries in the lower portion of the band. Thus the main difficulty in any operation for section of the band would seem to be in regard to the peritoneal processes and the portal circulation. The anastomosis which may exist between the internal mammary arteries and the intercostals in the integument in the upper portion of the band, of course would present no difficulty.

I will not venture upon any further remarks as to the surgery of the case, while there are so many distinguished gentlemen present more competent than myself to give an opinion. At the same time, operations on the peritoneum may not be considered so hazardous in this day, when ovariectomy, gastrotomy, and even Caesarian section, are so often performed. The peritoneal pouches themselves would not present so great a difficulty as might be anticipated, under pressure and acupuncture, by which the sensitiveness of the structure might be so altered as to permit of a section. I was informed at Mount Airy that in Paris a surgeon had made the experiment of applying pressure upon the band, and it was reported the twins had fainted in consequence. I could not ascertain, however, whether this was from fright, design, or actual pain.

As Dr Hollingsworth is present, it may be proper for me to mention a fact which that gentleman can corroborate, that Eng was the stronger physically and Chang was the stronger mentally. The same difference was observable in their characters. Chang was more irritable than Eng, especially since an attack of paralysis with which he had been afflicted,—this being in the side next to Eng.

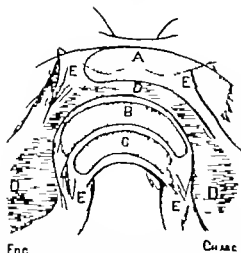


Fig. 3. Diagrammatic representation of the band. *A*, Upper or hepatic pouch of Chang; *E*, *E*, (dotted line) traces of the exsiform cartilages; *D*, connecting liver band, or the "tract of portal continuity"; *B*, the peritoneal pouch of Eng; *C*, the lower peritoneal pouch of Chang; *E*, *E*, lower border of the band.

The latter had not only to bear with the irritability of its associate, but also to support one half its weight. Among other peculiarities, Chang could sometimes break useful arteries or throw them in the fire.

In conclusion, let me say that when I turned up the skin and superficial fascia of the H incision on the posterior part of the band, I was struck with the development and the strength of the abdominal processes. The fibres arched, interlaced, and developed into strong fibrous bands about quarter of an inch wide, running around the median line, although there was no actual joint in the cartilage.

#### PROF HARRISON ALLEN

If *Chairman*, I will probably best discharge the duty devolving upon me by at once proceeding to a somewhat more minute anatomical description than Dr. Fancourt has given, this being in accordance with the understanding between us in reference to the evening exercises.

Perhaps it could be best to point to that simple diagram upon the blackboard before considering the subject more fully in detail. As Dr. Fancourt has informed the Fellows, there is union of the twines at the two exsiform cartilages,

which are very firmly joined in the centre. Eng's process being the more robust of the two. You will observe that there is a point of contraction between the two processes.

Which is not quit in the median line of the band. In the centre of the band is seen an elliptical space which suggests to the observer the presence of a synovial cavity. It is probable that the median junction is of the character of a synchondrosis, with median bands like our neither exsiform cartilage ossified.

Below this point in the diagram (Fig. 3) you see a number of differently lined tracks. The lower one (*C*) immediately above the umbilicus is only separated from the skin by a very delicate layer of tissue (so that, if the finger introduced into the pouch and moved, there is decided indication of motion in the skin) on the under surface (*E*, *E*) of the band.

This pouch passes across the band from the abdomen of Chang, and is lost in the duplicature of the suspensory ligament of the liver of Eng. The finger passed upward to the band from the abdomen of Eng crosses the band above pouch just mentioned, and is lost between layers of the suspensory ligament of the liver of Chang. When the significance of the round ligament at the free border of the suspensory ligament is remembered, the relations of three pouches directly suggest that they have had essential bearings to the umbilical vein of the foetus, and may be provisionally termed the *umbilical pouches*. Above Eng's pouch (*B*) and between it and the under surface of the exsiform conjunction, is second pouch (*A*) prolonged from Chang's abdomen, which fairly reaches the peritoneal cavity of Eng, but is not continuous with it. Extending up into this pouch from Chang's abdomen is a process which suggested to the Commission the possibility of the transit of hepatic nuclei. This view was rendered more probable from the fact that similar process passed up into the band from the liver of Eng. Accordingly the plates injection, colored by ultramarine as thrown into tributary of the portal vein of Chang, then it was observed that the fluid passed freely into the liver of Eng, as well as into some of the mesenteric veins proper. It is my own hypothesis that this band of colon (*D*) is the true hepatic tract, but in its present state is the absence of evidence of any paracymbiontic anastomosis about the vessels then crossing the band, precludes the transit as the tract of portal continuity.

In the foetal condition it is very likely that this large space (*A*), the upper pouch, now continuous with the abdomen of Chang only, is entirely occupied by true liver tissue,

which, as maturity is attained, became smaller and left an empty space. Hence I propose to call this upper pouch the *hepatic pouch*. The contraction changed it to be greater on Chang's side, in harmony, it may be with other evidences of weaker and less developed type, which is so apparent in many of the twines of Chang. Now with reference to the demonstration. As Dr. Fancourt has already informed you, the incisions in the abdomen are made in rather an exceptional manner. By reference to the parts it will be seen that the incision in either individual was located in such a way as to avoid the median line, where it is supposed from the peculiar position of the umbilicus that the remains of the hypogastric arteries could be found extending from the fœtus of the bladder upward and around along the entire length of the anterior wall of the abdomen. Besides, this incision could enable us, by continuing from below upward, to fairly open the abdomen and examine the cord, without violating the conditions by which the Commission are bound. The flap comprises the greater part of the abdominal wall, and can be best observed, from the position of the bodies on the table, as that of Eng.

You notice that the twines are well supplied with fat; and this condition is very plainly in contrast with that of Chang. Eng's side of the band is well described. Chang's end of the band presents an entirely different aspect. Chang was as feeble, and the weaker half of this organism, with less strength in the abdominal wall, and in every way less tissue than as possessed by Eng. You can mark that distinction very plainly in the two halves of the band, previous.

If I had an other means of proof that there could not be any cry intimate communication of vessels between them. The first point of entry of matter is that of an isolated mass of adipose tissue, evidently sub-peritoneal, which in the portion of the great twines, namely in the median line of the abdomen, about half-way up the anterior wall. This is strictly symmetrical, similar point of about the same size being found in Chang.

Another fact equally well pronounced is that in Chang the bladder was found very much contracted and contained no urine, it was deep down in the cavity of the pelvis. That of Eng, however, was distended with urine, hence there was a contrast in the appearance of the umbilical fold in the two individuals, in consequence of the bladder.

My finger is now in the *umbilical pouch* of Chang (C). The motion is noticeable in the under surface of the hand. On the side of Eng no such motion will be observed. I can very clearly see my finger passing between the two folds of the suspensory ligament. At this point it would perhaps be well to exhibit the drawings which have been made of the views which we have been able to obtain from this very limited incision. On looking up towards the hand with the greatest possible stretch of tissue, we see the arrangement of the remains of the hypogastric arteries converging towards the hand of union. In this lower diagram we show you the livers joined by what is supposed to be the *tract of portal continuity*. You will observe the limits are somewhat symmetrical. Here is the liver of Chang, with a fore-shortened right lobe.

The remainder of the right lobe is deep within the abdomen and of course it has not been seen. Here is the fundus of the gall bladder, and there the suspensory ligament, carrying the remains of the umbilical vein. When the finger is passed from Chang into Eng, it is received between the folds of the suspensory ligament of Eng. In Eng, the parts are essentially the same although you see more evidence of adipose tissue. Here is a little ligament aiding in the support of the liver, to whose convexity it is attached, it is not seen in Chang at all. You might term it an accessory suspensory ligament. When the finger is introduced behind the pouch, it is observed to terminate blindly, showing, we think, that it is adventitious, due to the presence of that suspensory ligament.

We find some vessels of the portal system even as far down as the mesentery, well filled with the blue coloring-matter. We of course desired, as far as possible, to examine all the tissues here by these incisions, hence it was that when the bodies were in this position the skin was taken off from the wall in order to get a view of the linea alba.

The bodies were here inspected by the audience, and afterwards turned so as to expose the posterior part of the band. Further remarks apply to this posterior aspect.

#### DR. PANCOAST

While the bodies are being turned, I will take the opportunity of replying to one or two questions which have been asked me. First, in regard to the common sensibility of these two individuals. According to the statements we received at Mount Airy, there was a line of common sensibility corresponding to the median line of the band. Dr. Hollingsworth says that if a pin were stuck into the hand at the median line, both of the twins would feel it distinctly, but that, even at the slight distance to either side, the point of the pin produced an effect only on the twin of that side.

Another question has been asked me, as to whether either of them was ever put separately under the influence of an anæsthetic. I answer it by saying that so far as we know it never was attempted but that when, upon the final occasion Chang was anesthetized by death, Eng was for a time unaffected. The story as told at Mount Airy was that Eng waked up and asked his son, "How is your Uncle Chang?" The boy said, "Uncle Chang is cold—Uncle Chang is dead." Then great excitement took place. Eng

commenced crying out immediately,—saying to his wife, whom they called in, "My last hour is come," and finally sank away. He was in perfect health when they went to bed.

They had been sitting up in a large double chair, made for their accommodation. Eng was smoking his pipe, until he became sleepy, and finally said to Chang, "We must retire." Chang said that he could not lie down comfortably. I understand that when they went from Chang's house to Eng's house (see editorial), where they died, it was against the direction of Dr. Hollingsworth, but with their usual stubbornness they persisted in riding in an open huggy. To return to the narrative of the night of their death, after Chang had refused to lie down, they walked about the house for some time, and even went out to the porch, and washed their hands and drank some water. It was about one o'clock when they went to bed. Then Chang died, some time between that and morning, his death not producing any immediate impression on Eng. It was only when the latter woke up and inquired about the condition of his brother, that he was at all affected.

As to the question, "What caused Eng's death?" I am not able to tell. The post-mortem which has been made does not show the condition of his lungs. Probably the valves of his heart were in a disorganized condition, and probably also the shock upon that weakened organ caused death.

#### DR. ALLEN

In my opinion, Chang died of a cerebral clot. From inquiry at his home, I was led to believe that the lung-symptoms were not due to pneumonia, indeed, were not severe enough to have been so caused. The suddenness of the death, the general atheroma of the arteries, and the fact that there had been previously an attack of cerebral paralysis, all indicated that the death was of cerebral origin. Eng probably died of fright, as the distended bladder seemed to point to a profound emotional disturbance of the nervous system, the mind remaining clear until stupor came on,—a stupor which was probably syncopal. One thing to be settled in the making of our examination was to get the bodies in the best possible position, so that we could judge of the true nature of the band.

You will observe the great contrast between the anterior appearance of the band and its posterior aspect. When we suspended them face to face we conceived we had them in the proper position for study. On the posterior side there was a fold underneath the skin extending from the ensiform cartilage of Chang, passing over, crossing the median line, and inserted into the ensiform cartilage of the opposite twin, Eng. It was one of the objects of the examination to determine what was the nature of the fold. I judge it to be the linea alba, but I leave the Fellows to decide for themselves. I will also add that, because we had not the privilege of cutting the anterior portion of the band, we were obliged to cut down from the point of which I have spoken to get to the structure, and demonstrate these *culs-de-sac* from behind.

Here (referring to the casts), from this point the incision is horizontal about midway, and joined laterally by two oblique lines which were directed one upward and the other downward and outward, making a modified letter-H incision. Thus we got all the space we needed. When I raised the skin, we see the scar of the umbilicus in the superficial fascia, and on lifting the other flap we get a better general demonstration.

And now we come upon the point of interest, namely, the position of the hand and its true nature. We have a diagram here. You notice on Chang's side that there is an

arrangement of interlacing spongy cartilage, marked here and there, starting in Chang, pass across the median line and are inserted into the enamel cartilage of Eng. Turning the lower flap downward, the upper flap upward, and the lateral tongues outward, the superficial fascia is exposed. This is abundantly supplied with adipose tissue on either side, but it is free from it here it covered the band. Both the lower flap and the fascia are lost in the scar marking the position of the umbilicus. The same dissection exhibits the position of the lower pouch of Chang. Turning down the external oblique, the two recti, and the internal oblique muscles, the transversalis was exposed, the latter forming a very well-defined layer in Eng, with an interval between the enamel cartilage and the anterior margin of the thorax. These were much less marked in Chang.

Turning forward this layer of fibres in Eng from without inward, the diaphragm is brought into view. Muscular fibres are conspicuous in this position. The peritoneum on either side is now fairly exposed. Incisions may now be made with view of demonstrating the pouches of the band. The upper pouch of Chang is, you will observe, freely opened on its posterior aspect, and the vessels in the tract of portal continuity are seen to be all distended with the injecting fluid. A small artery is seen crossing beneath this tract of veins, and is probably a branch of the hepatic, whatever may be its origin, it evidently could be of little effect in influencing the nutrition of parts beyond the band, and is probably retained within the band itself. The lower pouch of Chang reveals nothing which was not demonstrable from in front, and the same may be said of the single pouch of Eng; thus confirming our opinions of the construction of the band before the pouches had been opened from behind.

Dr. ARRAHAN JACOB, of New York, being called upon, said:

I am very much obliged to the gentleman who has mentioned my name. I do not believe Mr. Chamberlain, that I have anything to add to the stock of knowledge in regard to the subject before us. If I am to answer the question as to how this monstrosity originated, especially whether they became connected after having been separate or gemina, I should say that the idea has been given up by those whose opinions are entitled to weight. It is true that years ago such specimens are spoken of by D. Allon of Halle and a number of others have alluded to the idea that two such individuals might in embryonic life become united simply by adhesion, the result of their being located together in the embryo. I think it appears to me that at that period such a thing might be possible; but of course the union would be superficial one, not involving the deep organs.

We know that the first epidermis is formed about the end of the fifth week of embryonic life, and that after a time it is thrown off, so that the embryo of about seven or eight weeks is more loosely covered with the real epidermis than in the earlier period. The epidermis is thrown off a number of times until about the fourth month of utero-gestation, when it is finally perfected and remains intact. Now it is suggested that at those times when the epidermis is thrown off the connection takes place between the two individuals, —just as the connection takes place between the prepuce and glans, which is so often found adherent in the fetus in a number of new-born children.

There are evidences, which cannot forget, that such connections have taken place before the final epidermis is formed, and about the time when the earlier coverings are being thrown off the period when the internal organs, frequently implicated in such monstrosities, are already formed. There are few double monstrosities so well de-

veloped as this one. I think the records of about four hundred monsters have now been collected in the books and journals, but very few are of such complete nature as this. Everyone has heard of the Hungarian Twins, who lived to the age of twenty-one years, in the last century. Another pair of female twins, that resided in Germany about ten years ago, are described at the time, in the *Berliner Wissenschaft*. They are of similar nature. There are a case on record, in which division has been successfully attempted, but in those cases the connections are not so well developed as in the Siamese Twins. The connection was in the same neighborhood, but so early superficial, —of skin and subcutaneous tissue. One of the cases is recorded by Dr. Boeckh (*Virchow's Archiv*). Fortunately or unfortunately I do not know which, they were his own children. They are of the female sex. He separated them immediately after birth. One lived three and half days; and when the case as described in 1860, the other was six years old. In that instance the connection —three and half inches long —extended from the umbilical process to the umbilicus. The other case is described as early as 1689, by the old German author Knebel.

As far as the origin of twin monsters is concerned, I am certainly of those who are not of the opinion that individuals could get into such an intimate connection by growing together. Certainly the connection is an original one. I believe that the general opinion is now that one Graafian ovum may have two, or one even has its nuclei; and these finally may become the nuclei of an egg, be closed together, surrounded by the same material, forming a single complete ovum; and thus it may be that the twins are included in the same ovum. I think that this will explain also why the sex is always the same; —by the way they are all in both male and both female. They are made in twenty or twenty-five per cent of the cases.

Dr. H. C. WOOD has asked Dr. Jacob's question in regard to the Biddenden Sisters (an account of whom will be found in another column of this journal), as to whether they had been reported in the books on monstrosities.

Dr. JACOB:

I do not know anything about that.

Dr. P. VECCHIARI stated that an account of these sisters was contained in a small popular book entitled "Lesions Tétragénitales," published by Samuel Thomas, London, 660.\*

\*The Editor of the *Times* submitted to Dr. P. Vecchiari for an opportunity of inspecting the work. The account of the Biddenden Sisters is in a small short, and evidently not part of the original book, but has been placed in it apparently under the title of the work, and as others by the editor and contributors of the paper, but of course, impossible to decide with any accuracy what was put in the book.

None of the Fellows desiring to say anything further upon the subject, on motion, the College adjourned.

On Thursday, February 19, the Commission continued the autopsy upon the Siamese Twins, and made some important discoveries. They found that the two livers, which were supposed to be joined only by blood vessels, are one body, the parenchymatous tissue being seemingly continuous between them.

The so-called tract of portal continuity is apparently liver-tissue, but the point has not yet



# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE text of the *Mammotting* book, *Histopathology of the Peripheral and Central Nervous Systems* adheres strictly to the meaning of the title. The author's approach has been almost entirely anatomical one. Little clinical discussion has been introduced, and still fewer physiological facts. The textual material therefore accomplishes its aim without becoming hodgepodge. Apparently the author believes the subject of nervous histopathology alone to be enough for one volume.

This book is not particularly an easy one to read. It is very closely written, without wasted space, words, or illustrations. If it is a bit laborious, it is because it is so packed with facts and covers such large number of individual topics. A pathological entity known to the neuropathologist has been undeserving of at least brief discussion. If it because the book is so well organized, and because careful division of pathological states in the brain, cord, and peripheral nerves has been attained, the book loses the heaviness, which might at first seem ominous, without becoming choppy or disconnected in thought.

The outstanding feature of the book is its concise but amply sufficient treatment of the inflammatory, toxic, and degenerative diseases of the brain and spinal cord, subjects known to be of great interest to the author. It would be difficult to find a more adequate description of the histopathology in these diseases, often so difficult to relate to one another and the student should find the author's presentation clarifying.

This is a useful, informative book. Its illustrations are numerous and have been well chosen. A generous bibliography follows each chapter. JOHN MURRY

BORN IN TEXAS Hugh Young<sup>1</sup> comes from line of illustrious forebears. His grandfather Colonel Hugh Franklin Young, as famous Texas ranger. His father at the age of 26, was commissioned brigadier general, the youngest, so it is said, in the Confederate Army. His mother's brothers were captains in Stonewall Jackson's regiment, and his maternal grandfather Dr. Kemper was famous physician. It was in his workshop that Hugh Young became proficient in the use of tools.

His early childhood was spent in San Antonio, Texas. His education presents an interesting story

In kindergarten his interest in mechanics and art began under the guidance of his teacher Miss Lerner of whom he speaks affectionately. This interest continued throughout his life.

Later Hugh Young attended the San Antonio Academy, a private school started by Dr. William B. Seeley who instilled in him a predilection for Latin and Greek. He attended the Stanton Academy and due to the influence of Major Owens he became interested in the classics. At one time he thought he would like to study journalism, but soon gave up the idea for the study of medicine.

He entered the University of Virginia and received the degrees of B.A., M.A., and M.D. in 4 years, truly remarkable achievement. After he graduated from the University he returned to San Antonio and began the practice of medicine. Once embarked on this venture he quickly realized his limitations and concluded that he needed advanced medical training,

decision which prompted him to pursue further studies at Johns Hopkins Hospital.

Dr. Young's early experiences at the hospital are very interesting, some are amusing. They illustrate his keen interest in the patient and his illness. Likewise his determination to secure an appointment on the house staff—a task that most difficult to obtain—is worthy of note. His story of the period when Oler, Kelly, Welch, and Halsted were in the process of building up the medical school and their great interest in the younger men, and his description of the operating-room technique used then are illuminating.

One day in October 1907 while walking down corridor he almost collided with Dr. Halsted and apparently was very much embarrassed. Dr. Halsted paid slight, if any attention to his discomfiture, and there and then pointed him of the fact that he and Dr. Welch had decided that he should take over the department of genito-urinary surgery. Young remonstrated, saying he knew nothing about the subject, but Halsted replied that they were fully aware of this but believed he might learn.

Thus began a very interesting, productive, and fruitful career. Once he received the appointment he set about to master the subject. This resulted in journeys to Europe where he visited the various clinics and interviewed prominent urologists of the old world. Great credit is due Dr. Young for his important rôle in developing the specialty of urology.

Dr. Young's interest in instruments was probably due in part to his early mechanical training. One of his early cystoscopes had a retrograde vision and rather proud of his achievement he showed it to Dr. Nitze, the father of the cystoscope. The tongue

HISTOPATHOLOGY OF THE PERIPHERAL AND CENTRAL NERVOUS SYSTEMS. By George S. Henshaw, M.D. 64 pp. and 100 ill. New York: Paul B. Hoeber Inc., 1930.  
HUGH YOUNG—A SURGEON'S AUTOBIOGRAPHY. New York: Hoeber Medical Co. 1930.

lashing he received from Dr Nitze must have been a severe one. Nevertheless, thoroughly undaunted, he held his ground with Dr Nitze and a fist fight almost resulted.

Dr Young's war experiences were wide and intensive. He describes the program for combating venereal diseases, skin diseases, and infestations by various forms of animal life. Directly the program for the control of these diseases was established, Dr Young carried it out in all its details. Mastery of the venereal disease problem resulted in rendering aid not only to soldiers but also to the civil population.

With a dynamic personality such as Dr Young possessed, it was natural that he should have many interests outside the practice of urology. Thus in the winter of 1903 he took an active part in the legislation for the prevention of tuberculosis. Despite the interest of the Baltimore newspapers in the matter and their intelligent presentation of the question, and after committees of prominent physicians, such as Osler, Welch, Thayer, and others, had appeared before the Legislature in favor of the bills, they were defeated. Not in the least daunted by this setback, Dr Young, singlehanded, tackled the problem and succeeded in having the bills passed.

We next find him aiding legislation for the care of the insane in Maryland, and for many years he was the chairman of the lunacy commission. Later on when the City of Baltimore needed a municipal hospital he again took an active part in obtaining the necessary legislation.

Dr Young, always greatly interested in aviation, was one of the early airplane riders, and when the Maryland State Legislature created an aviation commission he was asked by his great friend, Governor Ritchie, to select members for the Commission, of which he became the first chairman. Other legislative activities included the "Purse-Netters" Bill and the Potomac River Bill. Recently he took an active part in preparing the exhibit for Maryland at the New York World's Fair.

He devotes 129 pages to the description of various urological instruments and surgical technique—a questionable procedure perhaps in a book intended for lay reading. The *Autobiography* reflects an interesting personality. Its style cannot fail to hold the reader's attention since it abounds with those enviable qualities—candor and simplicity.

HERMAN L. KRETSCHMER

THE author of *A Manual of Otolaryngology* follows the usual plan in dividing the subject into its four main parts. The anatomical descriptions are given at the beginning of each part and are followed by discussions of the etiology, symptoms, diagnosis, and treatment. While concise, the descriptions are clear and adequate, and the many illustrations are a great addition. The entire field is covered so well that it is difficult to select any outstanding part.

A MANUAL OF OTOLARYNGOLOGY. By Howard Charles Ballenger, M.D., F.A.C.S. Philadelphia: Lea & Febiger, 1940.

Osteomyelitis of the skull is well described by the method of taking each bone separately. A good comprehensive understanding of the subject is given in a few pages.

Functional hearing tests are carefully described and illustrated, so interpretations as to the type of deafness can be made with ease. The same applies to the functional tests of the labyrinth. Here the author includes an excellent, illustrated chart showing the vestibular reactions.

This book is an outstanding textbook of its type and should find a warm welcome with the undergraduate medical student and the general practitioner.

LINN F. MCBRIDE

LONG awaited, the radiological world gladly welcomes the appearance of the guide to the anatomical and roentgenological study of the head and neck by Pancoast and Pendergrass.<sup>2</sup> This work of nearly 800 pages, with over 1,200 illustrations, is most comprehensive. It is difficult to indicate any sections of unusual excellence, the entire work is a triumph of modern medical radiology, constituting a principal source of information on the radiological aspects of the head and neck for physicians, surgeons, and specialists who wish expert knowledge concerning the diseases, injuries, and anatomical variations of this part of the body. Praise must be voiced for the excellence of the illustrations, including a number of excellent anatomical drawings, displaying new aspects of anatomy as well as new information. Every possible phase of head and neck disease, injury, and anatomical variation is recorded, including radiology of the teeth and the localization of foreign bodies in the eye.

JAMES T. CASE

THE third edition of *Pathology*<sup>3</sup> appears, according to the author's preface, in two forms—as a separate textbook, the book now being reviewed, and bound together with a textbook on microbiology written in collaboration with Mrs. Jean Martin White (Piette and White *Microbiology and Nursing*, F. A. Davis Company, 1940).

The present edition of *Pathology* is in four units: general pathology, special pathology, tumors, and autopsies and clinical pathology. These comprise 18 chapters, and 229 pages of text, quarto. The indexing is good. There are 60 illustrations, almost all reprinted from other authors, none in color, (4 are partially colored), many of them apparently from drawings, and without explanatory pointers or labelling. These are almost without exception of very indifferent quality, and it is doubtful that they would mean anything at all to the student nurse, for whom this book is written, since they signify but little to an experienced pathologist. It is probable

<sup>2</sup>THE HEAD AND NECK IN ROENTGEN DIAGNOSIS. By Henry K. Pancoast, M.D., Eugene P. Pendergrass, M.D., J. Parsons Schaeffer, M.D., Ph.D. Springfield, Ill. and Baltimore, Md.: Charles C. Thomas, 1940.

<sup>3</sup>PATHOLOGY. By Eugene C. Piette, M.D., 3d ed. Philadelphia: F. A. Davis Co., 1940.



that these illustrations are not worth the space they occupy (It is but just to add that most are captioned with good explanatory notes in fine print.)

Each chapter is prefaced by an outline of its contents and concluded with a set of review questions. Both add distinctly to the usefulness and clarity of the text.

At the end of each chapter references are cited, these are largely a repetitious listing of the standard texts of pathology used in medical schools, and found on every pathologist's shelves. Since no page references to the subjects referred to are included, it is hardly to be expected that the student nurse will profit by the inclusion of these references. Space would be saved if most were omitted and unless page references were indicated, the list might certainly better be consolidated at the end of the book.

Most of the above criticism is of an adverse nature. The text, however, is written simply and covers economically and clearly as much of pathology as the nursing school curriculum permits. The textual portion of the book is excellent. The typography is large and lends itself to comfortable reading. Pedagogically the text could be improved by the addition of more short illustrative case reports (such as is cited on page 128) particularly those illustrative of the more important lesions.

The present reviewer considers this a good book, which will continue satisfactorily to fulfill the use for which it was written, namely as a text of pathology for student nurses. It is succinct, practical, and clear. Because the text is good the book deserves to be improved by illustrations of a quality which will complement the text.

FRANK B. CREEK.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

FRACURES AND DISLOCATIONS FOR PRACTITIONERS. By Edwin O. Glickler, M.D. 2d ed. Baltimore: The Williams & Wilkins Co., 1920.

A SCROGGS'S LIFE; THE AUTOBIOGRAPHY OF J. M. T. FERGUSON. New York: G. P. Putnam's Sons, 1920.

THE DIAGNOSIS AND TREATMENT OF DISEASES OF THE HEART. By Henry A. Christian, M.D., Sc.D. (Hon.), LL.D., F.A.C.P. Hon. F.R.C.P. (Can.) (Reprinted from *Oxford Monographs on Diagnosis and Treatment*). London, New York, Toronto: Oxford University Press, 1920.

HYDROCELE; ITS SYMPTOMATOLOGY, PATHOLOGY, PATHOGENESIS AND TREATMENT. By Ott. Marburg, M.D. New York: Oscar Reist, 1920.

THE 1920 YEAR BOOK OF PATHOLOGY AND INTERNAL MEDICINE. Edited by Howard T. Kassar, M.D. Chicago:

out edited by Sanford B. Hooker, A.M., M.D. Chicago: The Year Book Publishers, Inc., 1920.

THE 1920 YEAR BOOK OF INDUSTRIAL AND OCCUPATIONAL SURGERY. Edited by Charles F. Painter, M.D. Chicago: The Year Book Publishers, Inc., 1920.

L. EMMETT HOLT: PROGRESS OF CHILDREN'S DENTISTRY. By R. L. Davies and L. Emmett Holt, Jr. New York, London: D. Appleton-Century Co., 1920.

SCHEMATIC ANATOMY OF THE HEAD AND NECK. By John Finch Barakoff, M.D., and William J. McInerney, M.D. 2d ed. Baltimore: The Williams & Wilkins Co., 1920.

PSYCHIATRIC DICTIONARY WITH ENCYCLOPEDIA TREATMENT OF MODERN THINGS. By Leland K. Hinkle, M.D. and Jacob Shtinsky, Ph.D. London, New York, Toronto: Oxford University Press, 1920.

THE UROLOGIE IN EXPERIMENTELLE CHIRURGIE. Edited by Prof. Dr. H. Boenigheuer. GANZ UND TRENNUNG DER ROHR-GERÄTECHENUNG VON HARNSTENGE. By Dr. Edward Phleger and Dr. Hermann Friedrich. Leipzig: George Thieme, 1920.

## CORRESPONDENCE

### SURGICAL AND MEDICAL SUPPLIES NEEDED FOR GREAT BRITAIN

The Medical and Surgical Supply Committee, composed of 150 physicians and surgeons in principal cities throughout the United States, is urgently in need of instruments, dressings, biologicals, pharmaceuticals and equipment to be shipped to Great Britain for distribution among hospitals and medical field stations.

Complete operation units for general and traumatic surgery as well as special units for ear, nose

and throat plastic, brain, orthopedic; and genito-urinary surgery are desperately required.

Doctors are urged to send these materials immediately to the Medical and Surgical Supply Committee of America, 420 Lexington Avenue, New York City.

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# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### THE HUMAN CORPUS LUTEUM OF PREGNANCY

JOSEPH GILLMAN, D Sc, M B, B Ch (Rand), and H B STEIN, M Sc, M B, B Ch (Rand),  
Johannesburg, South Africa

**A** CORPUS luteum is found only in the ovary of mammals. Subsequent to the classical experiments of Fraenkel (1903), who demonstrated that the corpus luteum plays an important part in maintaining gestation in the rabbit, attention was rapidly diverted from the anatomy to the dynamic and perhaps more spectacular physiology of this body. This diversion has culminated in the isolation of progesterone and the techniques for assaying this hormone.

The structure of the human corpus luteum of pregnancy was being investigated in the first two decades of the present century by Rabl (1899), Seitz (1906), Meyer (1911), Miller (1914), and Marcotty (1914), but there has been no anatomical report since the comprehensive study of Moulouguet-Doleris (1925).

Investigations into the ovarian hormones have been in progress in this department of anatomy since 1932. When it was discovered that the human corpus luteum of early pregnancy was a cystic structure and that the cystic cavity contained a potent hormonal fluid (Gillman and Smyth, 1939) it was obvious that re-examination of the histology of the gravid human corpus luteum was also overdue. The anatomical approach, while laborious, was imperative if we were to correlate changes in structure with those of function in

the human corpus luteum. This study was facilitated by accumulating a comprehensive series of fresh human corpora lutea, removed at operation from cases of proved intra-uterine pregnancy at different stages of gestation.

In this paper we hope to demonstrate that there is a "critical period" of sudden growth in the volume of the corpus luteum between the fiftieth and sixtieth days of pregnancy due to an excess production of hormonal fluid in the fibrous-tissue-lined cavity, which is subsequently obliterated, that the theca-lutein cells attain their maximum development synchronously with the development of this curious cavity and that subsequent upon its collapse they too disappear, that the granulosa-lutein cells on the other hand persist throughout pregnancy and that their vacuolar secretion may degenerate into colloid and even solid calcium containing deposit. Curves will be presented displaying the relative incidence of cells containing lipoid, secretory granules, and colloid at the various stages of pregnancy typified by our specimens. Finally we have correlated the experimental, physiological, and cytological evidence bearing on the function of the corpus luteum of pregnancy.

#### MATERIAL AND METHODS

The corpora lutea from normal cases of intra-uterine pregnancy used in this study

TABLE I.—NUMBER AND DISTRIBUTION OF CASES OF GRAVID CORPORA LUTEA EXAMINED BY VARIOUS INVESTIGATORS

Author	Year	Operation specimens		Autopsy specimens	Total examined
		Intra-uterine	Extra-uterine		
Meyer	79				200
Müller	79				202
Marcotty	1914	3			187
Macdonald-Deloris	24, 25	41			5
Porter, Auchincloss and Raley	1918				71
Present authors		13		9	22

\*Marcotty: In two cases no data as to the origin of the specimens are available.

†24, 25 months.  
‡Macdonald-Deloris: It is not indicated whether these are all operation cases.

§Operative.  
||Porter, Auchincloss and Raley: No exact figures are given.

represent one of the largest series hitherto examined (Table I). With the exception of Marcotty investigators have not always divulged the source of their material and thus we are ignorant as to whether the corpora were removed at operation from individuals who had a normal intra-uterine pregnancy or ectopic pregnancy or whether the ovaries may not have been removed at autopsy.

We have found that corpora lutea removed from cases of intra-uterine and of ectopic pregnancy are not identical in structure since the corpus luteum undergoes involution when the embryo dies and it is unusual to find a living embryo in an ectopic pregnancy.

Again, in autopsy cases, as hereinafter indicated the lipid and colloid disappear from the corpus luteum. Specimens examined 24 hours after death present scarcely any colloid.

We described here, therefore only such corpora lutea as were removed at operation in cases of a proved intra-uterine pregnancy. The few autopsy and extra-uterine specimens are included in Table I only for comparison.

Of our 19 specimens no less than 13 were removed at operation from normal individuals in different stages of intra-uterine pregnancy: 2 were from operations for ectopic gestation, and 4 were from autopsies. Three of the autopsy specimens were from cases of accidental death and the fourth from a case dying of puerperal sepsis. Table II shows the dis-

tribution of our cases under three classes: namely (a) normal intra-uterine cases in which specimens were removed at operation; (b) ectopic cases in which specimens were obtained at operation, and (c) autopsy cases.

The age of the corpus luteum in operation cases has been estimated from the date of last menstrual period and in the autopsy cases from the size of the fetus according to the data collated by Argy (1930).

The specimens were fixed in 70 per cent neutral formalin and in addition small pieces were removed for cytological investigation. The description of which will be published elsewhere. Fragments of the formalin-fixed portions were subjected to the freezing microtome and sections cut for the investigation of lipids while the remainder of the specimen was dehydrated in alcohol and embedded in paraffin.

The frozen sections of each specimen were stained in routine fashion by the scharlach Nile blue sulphate, and osmium tetroxide methods for the detection of lipid and fatty acids. A fourth section was stained with scharlach R and counterstained by hematoxylin, while a fifth section was mounted in glycerine without staining and examined by means of polarized light for the detection of anisotropic lipid. Other sections were subjected to the Schultz microchemical technique for cholesterol. A concise description of the lipid methods is given by Carleton (1938) and was critically discussed for the gall bladder by Stern (1938).

The paraffin sections were stained as a routine with hematoxylin and eosin with Maltby's triple connective tissue stain, by the Bielschowsky Foot method for reticulum, and with toluidine blue for chromidial substance.

#### OBSERVATIONS

The earliest stages in the succession of morphological events in the corpus luteum man as it changes from a menstrual to gravid state are unknown. As no one has yet had the opportunity of examining the earliest corpora lutea of intra-uterine pregnancy our knowledge of this vital subject must necessarily be inadequate. But there are sufficient data available about the structure of the menstrual corpus luteum at the

TABLE II—SIZE OF CORPUS LUTEUM AND OF CENTRAL CAVITY, AND PERCENTAGE OF GRANULOSA-LUTEIN AND THECA-LUTEIN CELLS CONTAINING SECRETORY GRANULES, LIPOID, AND COLLOID DROPLETS IN 19 CASES OF PREGNANCY

Case No	Age (days)	Size (mm )	Size of central cavity (mm )	Granulosa lutein cells				Theca lutein cells	
				Secretory granules per cent	Lipoid per cent	Colloid droplets per cent	Cholesterol	Secretory granules per cent	Lipoid per cent
A.—Operative (uterine) cases									
1	c 35	10x 7	Coagulum	50	58	5	Traces	22	44
2	51	18x10	10x 5	40	95	6	Traces	50	47
3	53	22x18	15x10	31	70	15	Traces	26	56
4	63	20x15	15x10	38	41	10		31	51
5	75	20x 9	8x 6	36	23	11		25	22
6	77	18x10	13x 5	45	33	13	Traces	24	26
7	78	19x 9	Loculated	22	35	18	Traces	45	32
8	98	16x 7	5x 2	43	55	15	Traces	40	55
9	127	10x 8	Absent	29	21	11		Absent	Absent
10	135	14x 7	4x 2	16	18	23		29	67
11	280	8x 6	Absent	0.5	10	50		Absent	Absent
12	280	8x 8	Absent	2	9	39 (calified)		Absent	Absent
13	282	11x 5	Absent	20	7	59		Absent	Absent
B —Postmortem (uterine) cases									
14	c 110	11x 6	Absent	35	10	Not seen	Traces	25	24
15	c 130	8x 7	Absent	14	6	Not seen		10	37
16	Term	10x 5	Absent	nil	1	Not seen		Absent	Absent
17	Puerperal	6x 4	Absent	2	0.5	11 (calified)		Absent	Absent
C —Ectopic cases									
18	47	13x 6	4x 4	17	95	8		27	16
19	c.50	14x12	Coagulum	20	25	9		29	90

height of its activity and that of the corpus luteum in the second month of pregnancy to deduce the probable sequence of events

After rupture of the mature graafian follicle (corpus folliculare menstruationis of Aschoff) and expulsion of the ovum, the cells of the stratum granulosum, according to most investigators (cf review of literature by Asdell (1928), enlarge to give rise to the lutein cells

The site of follicular rupture heals by a proliferation of connective tissue which closes the stigma and converts the whole follicle into the maturing corpus luteum in which a central cavity persists as evidence of the original lumen of the graafian follicle. The corpus luteum grows in size mainly by a hypertrophy of the lutein cells. The mature corpus luteum of menstruation (corpus folliculare efflorescens

of Aschoff) is reached 14 days after ovulation when the corpus luteum may measure 18 by 12 millimeters. A hemorrhage now develops, originally in one pole of the lutein tissue (Fig 1, A) and later at several points, finally bursting into the coagulum of the central cavity, and resulting in a central fibrinous clot and obliteration of the cavity (corpus folliculare hemorrhagicum of Aschoff). Menstruation itself occurs soon after this event. This marks the commencement of the involution of the "menstrual" corpus luteum, connective tissue organization supervenes and the cells become infiltrated with lipid to produce the characteristic yellow color of the retrogressing corpus luteum (corpus luteum menstruationis of Aschoff). Later the cells degenerate, the lipid is removed by histiocytes and the scarring

TABLE III.—AREAS OF THE WHOLE GLAND LUTEIN TISSUE, FIBROUS LAYER AND CAVITY AT DIFFERENT STAGES OF PREGNANCY IN SQUARE CENTIMETERS

Case No.	Age (days)	Area of cavity (sq. cm.)		Area of fibrous tissue (sq. cm.)		Area of lutein tissue (sq. cm.)		Total area sq. cm. X 2.7
		Actual X 6.75	Per cent of total	Actual X 6.75	Per cent of total	Actual X 6.75	Per cent of total	
	351							
	37	61		292	75	379	43	643
	53	414	33	393		663	53	1,390
		678	57	690	64	76	27	1,395
	81							
6	77	1.26		299	26	367	63	643
	78	1.2			13	669	6	643
8	96	87	6	306	22	379		643
	37			16	6	330	64	368
30	115			76		379	86	627
	130			66		769	3	669
	160					14	66	179
3	161			8		373	91	130

\* Estimated from sections passing through the greatest diameter of the corpus luteum. † Obtain the actual area the figure must be divided by 6.75. ‡ and were slightly damaged at operation and are not included since complete sections passing through the middle of the corpus luteum could not be obtained.

process increases. The corpus caudicans (corpus follicular involutum of Aschoff) is thus formed.

In the second month of pregnancy the gland as a whole is larger than the corpus follicular efflorescens in consequence of the hypertrophy of the lutein cells and an accumulation of straw-colored fluid within the central cavity. The inner rim of connective tissue lining the deepest part of the corpus luteum by that time has increased considerably in thickness (Figs. 2 D and 17 D).

Instead of the hemorrhage which customarily occurs either immediately before or simultaneously with menstruation, the pregnant corpus luteum experiences probably a simple hypertrophy during the period between fertilization and implantation of the ovum.

We have attempted to express in a rough mathematical way the fluctuations in size of the corpus luteum throughout pregnancy. The simple procedure adopted for this purpose was to select the section passing through the greatest diameter of the corpus luteum the section was projected on graph paper at a magnification of 25 diameters and the whole corpus the lutein tissue, inner fibrous layer and the central cavity were outlined. The areas were then obtained (Table III) and

from this information Figure 3 was constructed. While this method is merely an assessment of relative size in comparing globoid bodies it was the only procedure we could adopt under the circumstances, since the tissue had been cut up according to plan for the specific techniques here mentioned. Nevertheless the results of this procedure reflect with sufficient accuracy for our purpose the progressive growth or diminution of the various parts of the corpus luteum during pregnancy. We have added for purpose of comparison a menstrual corpus luteum which was removed one day before the next expected period.

When fertilization occurs the corpus luteum scarcely grows in diameter and volume for the first 30 days of pregnancy (Fig. 3). Between the fiftieth and sixtieth days the corpus luteum doubles its premenstrual area as seen in cross section. By the eightieth day its area in section is once again reduced to that of the premenstrual corpus luteum and at term has become reduced to half the area presented by the premenstrual corpus luteum and a quarter the area of the "pregnant" corpus luteum at the height of its activity.

The enlargement during early pregnancy is produced chiefly by the formation of the fluid-

free from granules. Cells containing granules possess a well formed, oval, vesicular nucleus, vacuoles, as will be noted, are rarely to be seen, and, if found, are small in size. The granule-containing cells occur most abundantly in the middle and peripheral zones of the lutein wall and are much less numerous in those granulosa-lutein cells which occupy the inner zone where the most highly vacuolated cells are present.

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The percentage of cells containing secretory granules forms a fairly reliable index of the age of the gravid corpus luteum (Table II). Granules are most numerous during the first half of pregnancy when they occur in approximately over 30 per cent of the cells, at the end of pregnancy only 2 per cent or less of cells contain granules. In one specimen at term, however, 20 per cent of cells still contained secretory granules (Case 13).

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size is due to fusion of the droplets. Finally the cell may disintegrate leaving a colloid mass not surrounded by any recognizable cytoplasm so that the colloid appears to lie extracellularly.

With Mallory's connective tissue stain the colloid droplets may stain either red blue or yellow. With hematoxylin and eosin they generally stain a pale pink color but in two instances (Cases 12 and 17) they showed a marked affinity for the hematoxylin staining a distinct blue and suggesting the possibility of calcification (Fig. 14).

Colloid droplets are apparently very labile and are not found unless the specimen is fresh. Thus they were absent from the autopsy specimens except for the one case in which they had become calcified.

The colloid droplets develop within the vacuoles, and all stages may be seen from the vacuole to the fully formed colloid droplet. The peripheral rim first stains and later the whole vacuole (Fig. 15). At first the colloid stains a pale blue or yellow with Mallory's stain in this phase it may be reconverted into colorless secretion so that clear vacuoles appear within the stained colloid mass giving the whole a fenestrated appearance. If however the colloid stagnates within the cell it becomes a dense spherical mass which is colored a deep red with Mallory's stain. In the later course of pregnancy these dense spheres may become calcified (Fig. 14).

**4. Vacuoles** occur in the cells as colorless round spaces in the cytoplasm of the granulosa lutein cells. Like the colloid droplets they are absent from the theca-lutein cells.

In the early stages of pregnancy the cells containing vacuoles are exceedingly numerous, and, under low power especially in the neighborhood of the central cavity the sections have a moth-eaten appearance. Vacuoles may occur in any of the granulosa lutein cells but the cells occupying the inner third of the lutein wall adjacent to the fibrous lining of the central cavity are the most highly vacuolated (Fig. 17 C) and are obviously participating in an active secretory process.

The vacuoles first make their appearance in the cytoplasm as small nonstaining circular areas which gradually enlarge and fuse so that

the whole cell becomes filled with a large vacuole surrounded by a thin rim of cytoplasm. The nucleus is frequently pushed to the periphery and becomes wrinkled and hyperchromatic and even pyknotic. Where several cells lying together show such large vacuoles they resemble a gland like acinus.

Specimens from the latter half of pregnancy contain fewer vacuoles in contrast to the earlier actively secreting gland. The contents of the vacuoles have become progressively stainable and form the colloid droplets, which accounts for the progressive increase in the number of colloid-containing cells toward term.

**5. Chromidial substance** occurs as numerous filaments and triangular or club-shaped bodies in the cytoplasm of the granulosa and theca lutein cells. Owing to their great diversity in size and shape it was not possible to make a quantitative estimation of the relative number of cells containing this substance they are most numerous in the early months and decrease greatly in quantity in the later months of pregnancy.

#### COMMENT ON MACROSCOPIC APPEARANCE OF THE GRAVID CORPUS LUTEUM

The most remarkable feature of the corpus luteum of early human pregnancy is the development of a relatively huge fluid containing cavity within the center of the gland.

The cystic corpus luteum has been described thus far in only a few pregnant mammals. It was noted in the ovary of a pregnant gorilla (Saglik, 1938). Van der Stricht (1912) also described a transient cavity in the corpus luteum of the bat. Rabi (1899) first drew attention to the fluid filled cavity in the human corpus luteum of pregnancy. This was confirmed later by Seitz (1906) and Marcotty (1914).

With the exception of Shaw (1936) the cystic character of the corpus luteum is not described in English textbooks of gynecology and obstetrics. German textbooks, however pay attention to this phenomenon (Aschoff 1924, and Schroeder 1930).

The early increase in size of the corpus luteum is largely accounted for by the growth of the cavity and the accumulation of fluid. This is obvious from Table II where in Cases 3 and



Fig 1 Photomicrograph of a section through a corpus luteum removed 1 day before next expected menstruation. Note blood clot at one pole, A, and remains of cavity of original graafian follicle. Hematoxylin and eosin,  $\times 33$

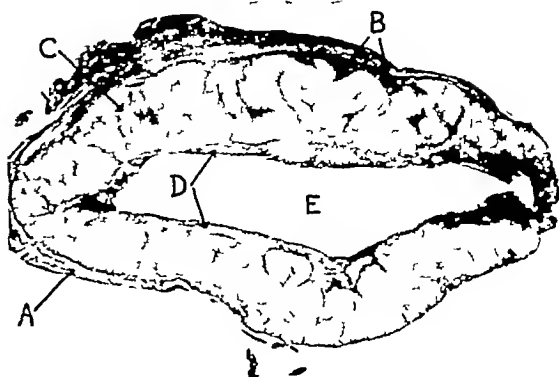


Fig 2 Photomicrograph of a section through a corpus luteum of a 77 day pregnancy (Case 6) A, capsule, B, theca lutein cells, C, granulosa lutein cells, D, inner fibrous layer, E, central cavity Hematoxylin and eosin,  $\times 33$

4, the cavity in a section through the largest diameter represents by area one-half of the corpus luteum. Further, when the cavity becomes smaller there is a diminution in size of the corpus luteum as a whole. The cavity reaches its maximum size, according to our observations, between the fiftieth and sixtieth days. Thereafter it diminishes in size becoming a tiny space (Case 10), or completely obliterated (Case 9) at about the fifth month. It is entirely absent at term.

Seitz, who made accurate measurements of human corpora lutea of pregnancy, found that the corpus luteum reached its maximum size

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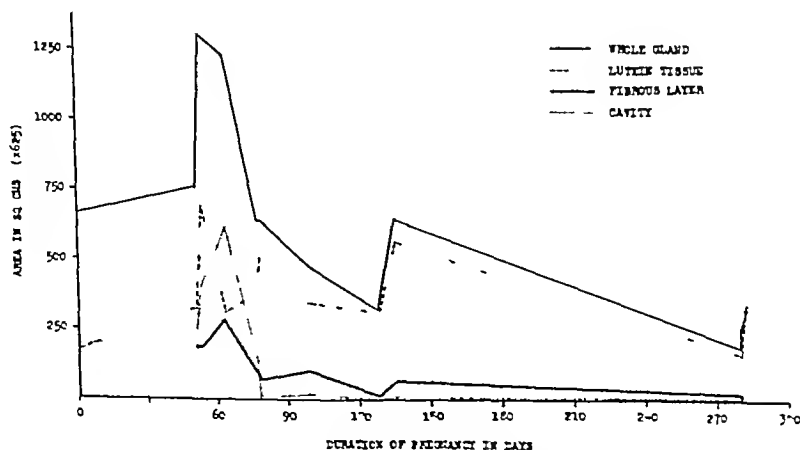


Fig 3 Graph showing area of whole gland, lutein tissue, fibrous layer and cavity at different stages of pregnancy. From data given in Table III

size is due to fusion of the droplets. Finally the cell may disintegrate leaving a colloid mass not surrounded by any recognizable cytoplasm so that the colloid appears to be extracellularly.

With Mallory's connective tissue stain the colloid droplets may stain either red blue or yellow. With hematoxylin and eosin they generally stain a pale pink color but in two instances (Cases 12 and 17) they showed a marked affinity for the hematoxylin, staining a distinct blue and suggesting the possibility of calcification (Fig. 14).

Colloid droplets are apparently very labile and are not found unless the specimen is fresh. Thus they were absent from the autopsy specimens except for the one case in which they had become calcified.

The colloid droplets develop within the vacuoles, and all stages may be seen from the vacuole to the fully formed colloid droplet. The peripheral rim first stains and later the whole vacuole (Fig. 15). At first the colloid stains a pale blue or yellow with Mallory's stain. In this phase it may be reconverted into colorless secretion so that clear vacuoles appear within the stained colloid mass giving the whole a fenestrated appearance. If however the colloid stagnates within the cell it becomes a dense spherical mass which is colored a deep red with Mallory's stain. In the later course of pregnancy these dense spheres may become calcified (Fig. 14).

4. *Vacuoles* occur in the cells as colorless, round spaces in the cytoplasm of the granulosa-lutein cells. Like the colloid droplets they are absent from the theca lutein cells.

In the early stages of pregnancy the cells containing vacuoles are exceedingly numerous, and, under low power especially in the neighborhood of the central cavity the sections have a moth-eaten appearance. Vacuoles may occur in any of the granulosa-lutein cells but the cells occupying the inner third of the lutein wall adjacent to the fibrous lining of the central cavity are the most highly vacuolated (Fig. 17 C) and are obviously participating in an active secretory process.

The vacuoles first make their appearance in the cytoplasm as small, nonstaining, circular areas which gradually enlarge and fuse so that

the whole cell becomes filled with a large vacuole surrounded by a thin rim of cytoplasm. The nucleus is frequently pushed to the periphery and becomes wrinkled and hyperchromatic and even pyknotic. Where several cells lying together show such large vacuoles they resemble a gland-like acinus.

Specimens from the latter half of pregnancy contain fewer vacuoles in contrast to the earlier actively secreting gland. The contents of the vacuoles have become progressively stainable and form the colloid droplets which accounts for the progressive increase in the number of colloid-containing cells toward term.

5. *Chromidial substance* occurs as numerous filaments and triangular or club-shaped bodies in the cytoplasm of the granulosa and theca lutein cells. Owing to their great diversity in size and shape it was not possible to make a quantitative estimation of the relative number of cells containing this substance; they are most numerous in the early months and decrease greatly in quantity in the later months of pregnancy.

#### COMMENT ON MACROSCOPIC APPEARANCE OF THE GRAVID CORPUS LUTEUM

The most remarkable feature of the corpus luteum of early human pregnancy is the development of a relatively huge fluid-containing cavity within the center of the gland.

The cystic corpus luteum has been described thus far in only a few pregnant mammals. It was noted in the ovary of a pregnant gorilla (Saglik, 1938). Van der Stricht (1912) also described a transient cavity in the corpus luteum of the bat. Rabl (1899) first drew attention to the fluid-filled cavity in the human corpus luteum of pregnancy. This was confirmed later by Sert (1906) and Marcotty (1914).

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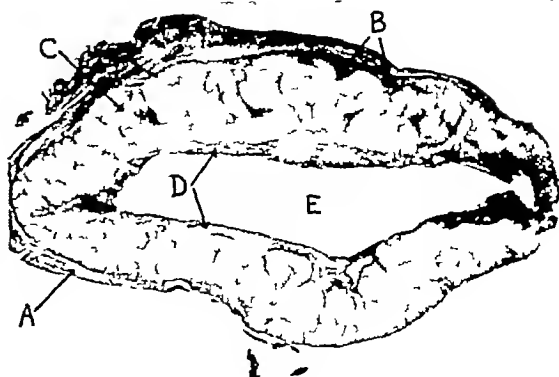


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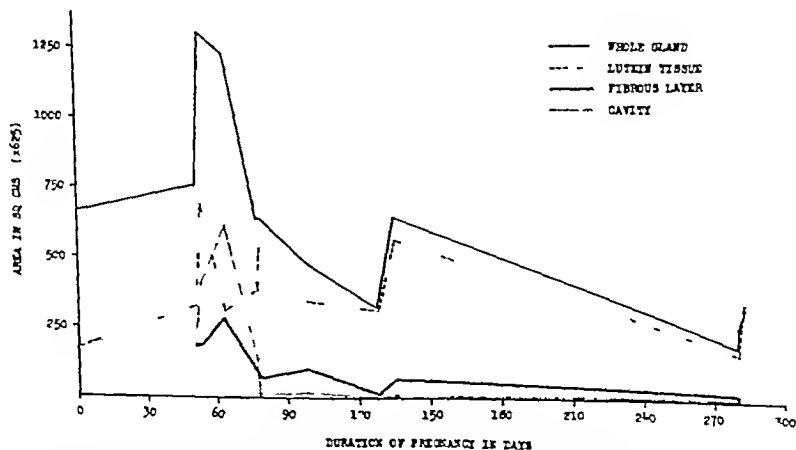


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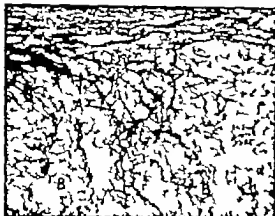


Fig. 4. Low power photomicrograph showing distribution of reticulum. Bielschowsky Foot silver method counterstained with neutral red, X97. A, theca lutein cells grouped in clusters by the reticulum, B granulosa-lutein cells with reticulum running irregularly between them.



Fig. 5. Low power photomicrograph to show general arrangement of theca lutein cells. A, round blood vessels, and granulosa-lutein cells, B Hematocytis and eosin, X97.

curve of the corpus luteum of pregnancy (Fig. 3) is only to form a basis upon which more comprehensive statistical examinations of the growth of the corpus luteum throughout pregnancy can be constructed.

The corpus luteum rapidly increases in size after the fiftieth day of pregnancy. This is maintained until the sixtieth day when it rapidly diminishes in size. The diminution is due to an obliteration of the central cavity and a diminution in thickness of the fibrous tissue immediately surrounding the cavity. The lutein tissue remains fairly constant in volume throughout pregnancy.

#### COMMENT ON MICROSCOPIC APPEARANCE OF THE GRAVID CORPUS LUTEUM

*Granulosa-lutein and theca-lutein cells.* The two component elements of the human corpus luteum have been known since the beginning of the present century (Pinto 1905). There is now unanimity of opinion as to the existence of the two cellular entities but controversy still rages as to their origin (Adelell 1928). The bulk of evidence is in favor of a separate origin of the theca-lutein and granulosa-lutein cells, the former from the theca interna and the latter from the stratum granulosum of the graafian follicle. We agree with this view.

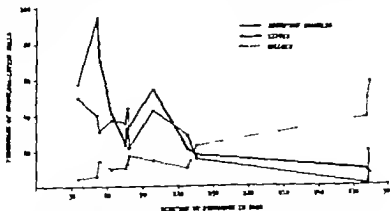


Fig. 6. Graph showing percentage of granulosa lutein cells containing secretory granules, lipid, and colloid at different stages of pregnancy. From the data recorded for 3 extra-uterine cases in Table II.

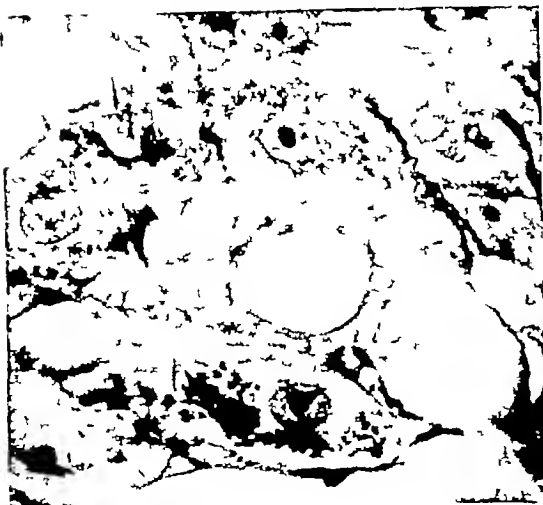


Fig 7 Oil immersion photomicrograph showing secretory granules in granulosa lutein cells Mallory's stain,  $\times 1345$

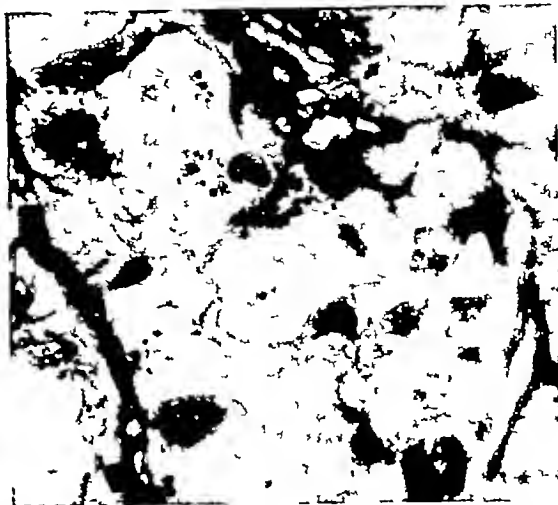


Fig 8 Oil immersion photomicrograph showing secretory granules in theca lutein cells Mallory's stain,  $\times 1345$

theca-lutein cells have not been found to metamorphose into the granulosa-lutein cells.

The theca-lutein cells are very prominent in the early months of pregnancy. In a single section passing through the center of the corpus luteum we find that thecal cells form as much as 8 per cent of the total area of the lutein tissue. As pregnancy advances the theca-lutein cells diminish in number until after the fifth month, then they disappear completely. In this respect the theca-lutein cells in the corpus luteum approximately parallel the growth and atrophy of the luteal cavity.

It is advantageous to mention here that a rhythmic formation and atresia of graafian follicles proceeds in the ovary throughout pregnancy. In the atretic follicles the theca interna cells enlarge and replace all other cellular elements. The degree of thecal cell-activity is generally more intense than occurs in atretic follicles encountered in the ovary during the menstrual cycle. The enlarged thecal cells in atretic follicles during pregnancy are indistinguishable structurally from the theca-lutein cells of the young gravid corpus luteum. Long after the theca-lutein cells have disappeared from the gravid corpus luteum, enlarged thecal cells are still to be found in these atretic follicles.

The granulosa-lutein cells are the typical glandular elements of the corpus luteum. Their general structure is sufficiently well known not to merit further description. One feature, however, needs more careful examination.

Some investigators have suggested that the darkly-staining and lightly-staining cells, which normally occur in the gravid corpus luteum, are indeed two distinct cell types. Corner (1919) has even described a third type in the pregnant sow.

Dark and light cells are present in every organ whether exocrine or endocrine. The nature of the dark cell in different glands may vary. Thus in the suprarenal and parathyroid the dark cells are known to be storage phases which ultimately degenerate in a large percentage of cases. In the goblet cell of the bowel and trachea they were found to be exhausted cells (Gillman, 1939).

In the corpora lutea from ectopic pregnancies in which fetal death had occurred, the proportion of dark cells is recognizably increased. The evidence from other tissues suggests that the dark and light cells in the corpus luteum merely represent different phases of secretory activity in the granulosa-lutein cells. As in other organs, many of the dark luteal cells ultimately degenerate.

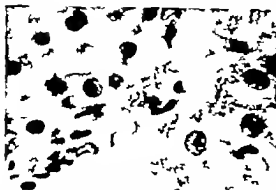


Fig. 9. Oil immersion photomicrograph to show fat droplets in the granulosa lutein cells. Lipoid is seen in the theca lutein cells in this region, one theca-lutein cell shows mitotic figure. Frozen section, Scharlach R and hematoxylin, X400.

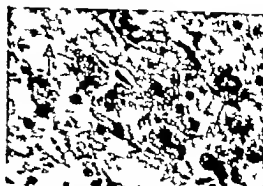


Fig. 10. Photomicrograph showing scattered granulosa-lutein cells laden with discrete lipoid droplets. A. H&E stain, bright red. B. Scharlach R and are frequently anisotropic (see Figures 1 and 2). Frozen section, Scharlach R and hematoxylin, X50.

**Nucleus.** Khvatov (1938) claimed that the nuclear size of the lutein cell in the rabbit tends to increase during pregnancy. We have measured one hundred nuclei in each of 3 cases, at the beginning, middle and the end of pregnancy. The average size of the nucleus (and the standard deviation) was as follows: Case 4, 63 days,  $11.8 \pm 1.3 \mu$ ; Case 10, 135 days,  $12.1 \pm 2.5 \mu$ ; Case 11, 180 days,  $10.9 \pm 2.3 \mu$ . There is thus no correlation in man between nuclear size and the length of gestation.

**Secretory granules.** As far as we can ascertain from the available literature the red tinted granules seen in the theca-lutein and granulosa-lutein cells, after staining with Mallory's connective tissue stain, have not been described in the human corpus luteum. These granules are not specific for pregnancy, as they have been observed in corpora 2 or 3 days before the onset of menstruation. They occur especially in the early months of pregnancy, where 50 per cent of the cells contain some granules, and gradually diminish until toward the end of gestation when only 2 per cent are granulated cells.

**Drips.** (1919) using the Altmann technique for mitochondria found granules in the corpus luteum of the spermophile in the early stages of pregnancy. On account of the technique used by her it is not clear to us whether these granules in the spermophile are mitochondria, secretory granules, fat, or a mixture of the

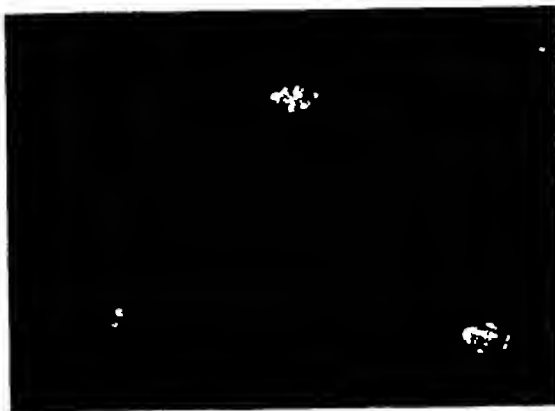
three. Drips states that in the late stages of pregnancy lipoid droplets appear which become abundant at birth. Following perhaps the lead given by Van der Stricht in his study of the bat, she believes the secretion of the lutein cells to be serous in the first half of pregnancy and lipoidal in the second half.

The secretory granules in the human corpus luteum are almost entirely absent from cells containing big vacuoles or colloid droplets. It has not been possible to establish the fate of these granules, but they may be the precursors of the nonstainable secretion in the vacuoles of the highly active cells. We have not been able to demonstrate with confidence their transformation into such secretion. They certainly do not give rise directly to the colloid droplets.

**Lipoid.** Meyer (1911) first described the presence of lipoid in the corpus luteum of pregnancy. Miller (1914) who considered all fat to be neutral fat, found no evidence of its existence in the gravid corpus luteum except during the puerperium.

Owing to technical difficulties existing at that time these observations are not entirely free from criticism. Meyer used the Sudan staining method on paraffin sections, while Miller regarded the Sudan staining without preliminary chroming as a technique for demonstrating neutral fat only and not for lipoid.

Marcotty (1914) appears to have been the first to use methods which are approved as



Figs 11 and 12 Photomicrographs of the same scharlach R stained section in ordinary light and under polarized

light (crossed Nicol's prisms) to show anisotropic lipid  $\times 315$

techniques for the identification of lipid, namely, Sudan III and polarized light applied to frozen sections, in addition to the now discarded Nile-blue-sulphate method. He found that young corpora lutea contained much fat in the theca-lutein cells and less in the granulosa-lutein cells. Later in pregnancy this distribution is reversed and the granulosa-lutein cells then contain more fat than in the early months. From the third to the seventh month very little fat is present. After the eighth month, however, the fat reaction becomes marked and this is further intensified during the puerperium. Some of these fat droplets according to Marcotty, were anisotropic under the crossed Nicol's prisms, he mentions the presence of such doubly refractile bodies in the early specimens, but not for the later specimens.

Moulonguet-Dolers (1925) found fat to be present only very early in pregnancy, diminishing considerably after the second month. He, therefore, considered that the gland functioned only early in pregnancy. He regarded the fat staining of sufficient significance to distinguish between the corpus luteum of pregnancy and that of menstruation. The fat in the gravid corpus luteum is labile being inconsistently soluble in xylol after osmication, the major part of it was anisotropic, and it formed characteristic pools or lakes, showing a diffuse impregnation with the fat stains. That of the menstrual corpus luteum however was stable, isotropic, and occurred as fine droplets.

There is thus in the literature considerable uncertainty as to the qualitative and quantitative distribution of luteal cellular fat at the various stages of pregnancy. Our own observations indicate that the number of fat-containing cells is much greater at the beginning than at the end of pregnancy (Table II), and that fat is found at least in some cells throughout the entire course of pregnancy. The fat generally occurs as fine droplets, these may later fuse and give rise to large globules. The accumulation of large discrete lipid droplets in isolated granulosa-lutein cells (1 to 5

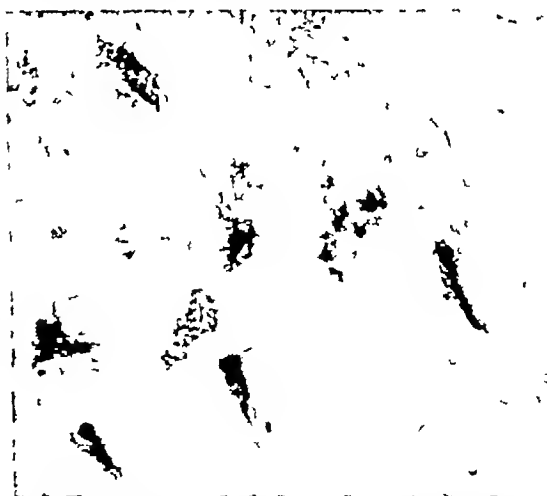


Fig 13 Photomicrograph of another frozen section from the same case as Figures 11 and 12. Treated by the Schultz method to show the greenish blue deposits of cholesterol appearing black in the photograph.  $\times 358$

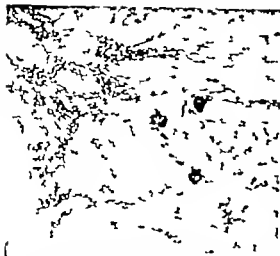


Fig. 4. Low power photomicrograph to show absence of theca-lutein cells and calcification of colloid at term (Case 1). Hematoxylin and eosin,  $\times 5$ .



Fig. 5. High power photomicrograph to show the evolution of the colloid droplet from the nonstaining secretion in acroses. From case 98 days pregnant (Case 8). Mallory's stain,  $\times 475$ . A nonstaining vacuoles; B peripheral staining of acroses to form colloid; C colloid with acroses in it; D fully formed colloid.

per low power field) is characteristic of the corpus luteum of early pregnancy. Such cells are apparently similar to the granulosa lutein cells of the involuting menstrual corpus luteum in the latter however the whole gland is composed of these lipid-laden cells. In the gravid corpus luteum the lipid of these isolated cells is also frequently anisotropic and Schultz positive for cholesterol thus cholesterol was detected only as traces in 7 of our cases in the granulosa lutein cells of the first 5 months of pregnancy. The relative absence of cholesterol throughout pregnancy is characteristic of the gravid corpus luteum the impression given by textbooks that the corpus luteum next to the adrenal, is the greatest site of cholesterol deposition is based on the examination of corpora lutea undergoing retrogression during the menstrual cycle. Visible cholesterol is not found to any extent in the actively functioning corpus luteum of pregnancy and the traces that are found probably represent a degenerative phenomenon of highly active granulosa-lutein cells, which have failed to recover at the end stage of the secretory cycle.

**Colloid droplets calcium and vacuoles.** Colloid droplets in the corpus luteum of pregnancy were first described by Rabl (1899) and later by Pinto (1905) and Seitz (1906). Miller

(1914) found them to be present in 22 of 23 cases and was the first to draw attention to their value as a criterion diagnostic of the corpus luteum of pregnancy. According to Miller their quantity showed no relationship to the duration of pregnancy the largest amounts were found in 2 cases of the first and third months and in a case during the puerperium.

Miller cited by Marcotty was also the first to draw attention to the fact that calcified droplets were frequent in the pregnant corpus luteum having found them in all his cases, with the exception of one in the second half of pregnancy.

Marcotty (1914) never saw colloid droplets in the corpus luteum of menstruation, whereas he found them in nearly every case of pregnancy. On analyzing the protocols submitted by Marcotty we noticed that those cases of corpora lutea of pregnancy which he stated contained no colloid were autopsy specimens. Our observations show that the colloid is very labile and is very susceptible to postmortem autolysis. Colloid droplets are described by Marcotty as being most abundant in the first to third months, diminishing in the latter half of pregnancy.

Marcotty described calcified bodies in 6 corpora lutea toward the end of pregnancy and in 2 during the puerperium.

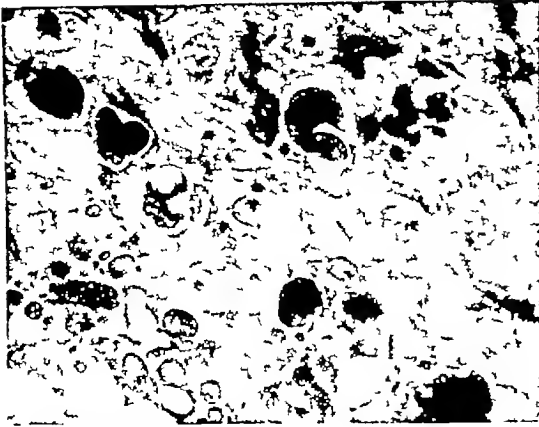


Fig 16 High power photomicrograph to show excessive amount and nature of colloid occurring in the corpus luteum at term (Case 11) Mallory's stain,  $\times 475$

Portes, Aschheim, and Robey (1938) found colloid droplets in every case of pregnancy, but never in the "menstrual" corpus luteum, and they suggested that this fact may be used as medicolegal evidence for the diagnosis of pregnancy. They regarded the colloid droplets as evidence of an active secretory process because (a) no accompanying cellular degeneration (lysis and pycnosis of nuclei) was seen within the cells where colloid droplets are found, (b) it appeared in the early gravid corpus luteum, which was undergoing marked functional activity and its presence was indispensable for maintaining gestation, and (c) they are not more abundant at term and during the puerperium than in the early months of pregnancy.

We are unable to accept this suggestion as we have found a quantitative increase throughout the course of pregnancy (Table II) and all the cytological evidence available strongly suggests that the cells containing big colloid droplets are inactive and many are even degenerated. We are led to conclude that the colloid droplets represent a stagnation of the secretion which, in the early cases, appears as nonstainable vacuoles in the cell. The calcified bodies are in our opinion merely a further stage of degeneration of the stagnant colloid droplets.

We may represent the sequence of events involved in the evolution of the colloid droplets as follows

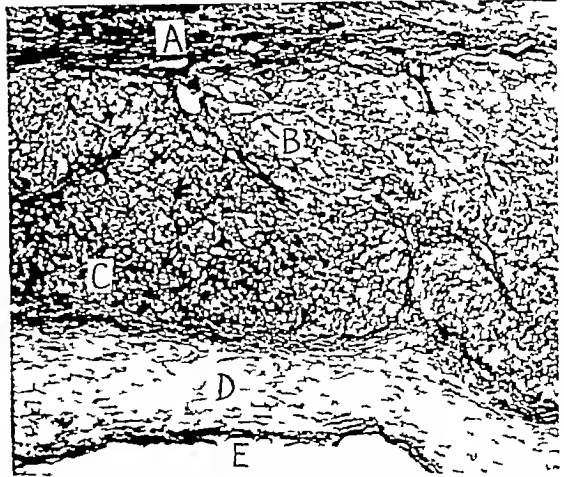


Fig 17 Low power photomicrograph to show the marked vacuolation of the granulosa lutein cells occupying the inner third of the lutein wall in early pregnancy (Case 4) Mallory's connective tissue stain,  $\times 38$  A, capsule, B, theca lutein cells, C, vacuolated granulosa lutein cells, D, inner fibrous layer, E, central cavity

Vacuoles (non	→	Colloid droplets	→	Calcium bodies
stainable		(stainable		(calcification
secretion of	←	secretion tend-		of the colloid
highly active		ing to stagnate		droplets =
cell)		in the less		degeneration)
		active cell)		

The colloid droplets are probably not completely degenerative secretory products except when they become calcified, and it is possible that the less dense, colloid droplets may be absorbed by becoming reconverted into the nonstainable substances seen in the phase of vacuolar formation. The value of the colloid as a medicolegal test, as suggested by Portes, Aschheim and Robey, is lessened when one considers that it is so labile to postmortem changes, except when calcified.

Since the time that Miller first described colloid droplets in the pregnant corpus luteum, it has always been regarded as characteristic of pregnancy. Colloid droplets have never been seen in the "menstrual" corpus luteum. One of our cases of a corpus luteum removed at the height of activity on the day prior to the next expected menstruation showed the presence of colloid droplets in 0.75 per cent of cells. The possibility still exists that this corpus luteum may have been associated with a very early pregnancy. If this should not be the case then the most reliable

diagnostic criterion is still the increased number of colloid containing cells since the lowest percentage recorded for our early pregnant corpora lutea was 6 per cent (Table II) whereas in this case there were only 0.75 per cent of colloid containing cells. In the post mortem specimens, however on account of the greater lability of the colloid even this quantitative test is of little value.

#### THE FUNCTION OF THE CORPUS LUTEUM OF PREGNANCY

The function of the corpus luteum of pregnancy has been investigated mainly by adopting two methods experimental and histological.

*Excision of the corpus luteum.* Largely as a result of the classical experiments of Fraenkel on rabbits in the early part of the century the opinion became established that the corpus luteum is indispensable for the maintenance of pregnancy. As more and more different species of animals were used for experiments it transpired that whereas in some animals the corpus luteum was necessary throughout gestation, in others it could be removed at some period without interfering with the pregnancy.

Removal of the corpus luteum causes abortion in the squirrel (Drips, 1919) and in the goat (Drummond Robinson and Asdell 1926). Corner (1928) showed that when bilateral oophorectomy is performed in the rabbit 14 to 18 hours after mating (4 to 8 hours after ovulation) ova develop to the blastocyst stage but the uterus does not undergo post-gestational proliferation and the embryo consequently dies. It is common knowledge that, in the rabbit castration after the twentieth day is not necessarily followed by abortion. Robson (1937) found that abortion occurs in hypophysectomized pregnant rabbits however if progesterone is administered to such animals, the pregnancy is not terminated.

On the other hand in the mouse the presence of corpora lutea is essential throughout pregnancy (Parkes 1928). Castration before the fifteenth to sixteenth day leads to absorption of the embryo after the fifteenth to sixteenth day abortion is precipitated with an unusually high percentage of stillbirths (Harris, 1927).

In pregnant guinea pigs Herrick (1928) discovered that castration at various periods caused abortion in the majority of his animals (15 of 18) but it was possible for pregnancy to continue if the ovaries are removed even before the middle of the gestation period.

Bilateral oophorectomy in the pregnant mare on the two hundredth day also does not necessarily interrupt the pregnancy as a foal was born on the three hundred and forty seventh day (Hart and Cole 1934).

Courner and Gros (1935) observed that in the cat with a normal gestation period of 64 days, abortion did not occur if the castration was performed after the forty-ninth day. Implantation occurs on the thirteenth day and if oophorectomy is practiced between the fifteenth and forty fifth day pregnancy is always terminated.

The recent work of Hartman (1939) shows that excision of the corpus luteum of the pregnant monkey even on the thirty first day of gestation did not produce abortion.

In the human female removal of the corpus luteum during pregnancy has been practiced. Sumner and Robey (1939) have reviewed some of the available literature on this subject. These are set out in Table IV.

TABLE IV

Author	Year	No. of Cases	Duration of pregnancy	Result
French and Vancura	19	10	First month	Nd
Ask Gynark	1926	21	First month	Nd
Fratt	1927		10th and 20th day	Nd
Waldman	1929		10th day	Nd
Mason Turner	1923		10th and 16th days	Nd
Benson and Kravitzka	1924		10-15th day	Nd
Bredesen and Heston	1925		Second month	Nd

From Sumner and Robey (1939).  
According to an abstract in J. Obst. & Gynaec. Brit. Emp. 1937  
24 of 25 cases Jones and Weil, 1938, there were 2 abortions and one was not recorded by Sumner and Robey.

Douglass (1931) reported the persistence of pregnancy after excision of the corpus luteum 4 weeks after the last menstrual period, while Corbet (1932) reported a similar result in a pregnancy of 42 days duration. Later Jones and Weil (1938) described a case going on to term despite the excision of the corpus luteum on the fifty-eighth day of pregnancy.

On the other hand De Lee (1916) reported 2 cases and Wilson (1937) 5 cases in whom excision of the corpus luteum resulted in abortion

Asdell (1928) collected 34 cases from the literature in whom bilateral ovariectomy was performed from the first to the seventh month of gestation and found that only 4 aborted. Asdell points out, however, that only those cases which oppose the view that oophorectomy produces abortion have been considered sufficiently interesting to warrant publication.

Despite this objection raised by Asdell there are sufficient cases on record to indicate that removal of the corpus luteum in the human female does not necessarily precipitate abortion. Obstetrical literature reveals that there has been a growing acceptance of the fact that removal of the corpus luteum in the second half of pregnancy is unlikely to interfere with gestation, but it now appears as if the removal of the corpus luteum very early in pregnancy also may not affect the normal progress of the pregnancy.

*Histological* The histological approach to the elucidation of the function of the corpus luteum has not proved very attractive to investigators. The general attitude up to the present has been that the corpus luteum of pregnancy is merely a more active corpus luteum than that encountered normally in the second part of the menstrual cycle, that it increases for a variable period in the early stages of pregnancy and then involutes and disappears. These views find expression in most textbooks on obstetrics.

From a review of the data set forth in the body of this paper the central feature that emerges is the extreme activity of the corpus luteum in the first and second months of gestation, the corpus luteum then reaches its maximum size, the percentage of cells containing the secretory granules and lipoid is maximal, and colloid is present in only a small percentage of cells (Table I and Fig 6). After that period there is a fairly rapid decline in all those features which are usually encountered in an active gland. One peculiarity of the early corpus luteum of pregnancy has particularly impressed us, namely, the development of the cystic cavity filled with what must be

regarded as a very potent hormone-containing fluid (Gillman and Smyth, 1939).

This cavity is enclosed not by epithelium or blood vessels, but, on the contrary, by a thick wall of seemingly edematous, fibrous tissue. This structure of the cyst wall is enigmatic, since, if the fluid were required by the organism, it is peculiar that such a strong wall should have been thrown down around a much needed secretion. Nowhere else in the whole body is there to be found a mechanism of this type elaborated for facilitating absorption! We know from what obtains in other endocrine glands that the absorbing cells are in most intimate contact with the circulation. The general cytological arrangements in other endocrine glands are such as would appear likely to facilitate the transport of secretion directly from the cells or fluid-containing cavities into the circulation.

In the corpus luteum on the other hand this very active secretion is walled off, so to speak, from the general circulation.

An important point in solving this riddle is the appearance in time of the potent hormonal fluid and the fibrous tissue around it. Is the dense fibrous layer present before the accumulation of fluid reaches a maximum, or is it laid down only after the maximal production of fluid has been reached?

If, for argument's sake, we accept the former view we must indeed wonder why nature has placed such an efficient barrier in the way of the passage of secretion to the central cavity. The cavity is largest when secretory granules, lipoid droplets, and nonstainable vacuoles are maximal and colloid droplets minimal, it disappears at the fifth month when the ratio of these inclusions becomes reversed. On this hypothesis secretory activity necessarily takes place across a barrier of fibrous tissue and we would therefore have to interpret the function of the corpus luteum as follows

secretory activity in ascendancy	to 60th day	secretory activity declining	to 130th day	involu- tion	to term
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If, however, we take the alternative view that the fibrous tissue is laid down only after the maximal production of fluid has been reached, and that the function of the fibrous



tissue is to wall off a surplus of secretion which is not required by the organism then we would have to interpret the function of the corpus luteum as follows:

secretory activity in ascendancy and secretory activity in decline	to 60th day	involu- tion	to term
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What is the state of the luteal cells in such corpora lutea as contain abundant luteal fluid? The histological criteria point to their being in a state of great functional activity as evidenced by the numerous secretory granules, the huge nonstainable vacuoles in the cell, the massive quantities of fine lipid and also by the state of the Golgi apparatus which is so huge as to be unparalleled in size by any other Golgi apparatus including even the motor nerve cell. Even though these cells are obviously in the throes of great secretory activity a large quantity of secretion is accumulating in the cells as nonstainable substances in the form of vacuoles and later as the stainable colloid droplets, the latter increasing progressively in size and numbers. It is clear that the stimulus for elaborating secretion is being continually applied in the early weeks of pregnancy and that the cells are responding in an excessive manner. Whether any of this secretion is poured directly from the cells into the circulation is difficult to say but there is abundant evidence that quite a considerable amount of the secretion is being stacked up in the cells.

There are two processes in the secretory cycle of the glandular cells: the first is the elaboration of the secretion by the cell and the second is the discharge of the secretion from the cell. These processes must be dependent upon two different and antagonistic or synergic stimuli for we know that cells can form their secretion but are unable to discharge it until the appropriate stimulus is applied. This is seen for example in the acinar cell of the pancreas, where the zymogen granules may crowd the cell but are only discharged when required.

In some endocrine glands, the thyroid for example, the discharged secretion may be stored for some period in follicles lined by epithellium. These follicles are big or small and the size of the follicles depends upon two

factors, namely the rate of formation and the rate of absorption of the secretion. If the thyroid epithellium is forming its secretion and discharging it, as is generally thought, into the follicle and if the absorption is proceeding at the same rate as its formation, then clearly there will be no increase in the size of the follicle. If however the secretion is being formed at a much greater rate than it is being absorbed then obviously the thyroid follicle increases in size. The formation of cysts in the thyroid and pituitary as well as in other endocrine glands seems largely dependent on these two factors.

If we apply to the corpus luteum around the fiftieth to sixtieth day interval of pregnancy the principles which seem to apply to endocrine glands like the thyroid and the pituitary we see that the luteal cells are highly active; they are obviously forming the secretion which is accumulating in the cells in the form of vacuoles and even of less easily absorbable colloid. Some of this secretion may be poured into the circulation but a great deal of the secretion is also accumulating in the central cavity where it becomes walled off by a layer of connective tissue which either excludes the secretion from the circulation or allows it to enter only very slowly. In short the secretion is unnecessary to the organism at the fiftieth to sixtieth day. This circumstance appears to us to explain the accumulation of the fluid and the development of its surrounding fibrous wall.

The conclusion we have drawn, therefore, from the histological features of the corpus luteum is that the luteal secretion poured into the central cavity is probably not required (from between the fiftieth and sixtieth days) in the quantity it is elaborated.

Excision experiments in the human female and in monkeys show that, at least in a large number of well authenticated cases, the corpus luteum is not really essential even in the early phases (50 to 60 days) of pregnancy. The histological appearance of the early gravid corpus luteum in our own opinion corroborates the conclusion which might be based on those experimental findings.

*The critical period during pregnancy.* The structure of the corpus luteum undergoes

important modifications from the fiftieth to eightieth days of pregnancy. At this period other important reactions are taking place in the body.

Thus Browne and Venning (1936), and Evans, Kohls and Wonder (1937) found that the excretion of gonadotropic substances in urine rose sharply between the fortieth and fiftieth day after the last menstrual period. The maximum concentration of this hormone occurred between the fiftieth and sixtieth day and then fell rapidly between the sixtieth and eighty-fifth day and then more slowly to the one hundred and twentieth day being thereafter maintained at this low level. MacGregor and Stewart (1939) however, found that the excretion of gonadotropic substance rose slightly toward term.

Pregnandiol glucuronide is excreted in the urine of pregnant women. It is regarded as an inactive product of progesterone. MacGregor and Stewart showed that in a normal pregnancy the pregnandiol excretion is relatively high between the sixtieth and eightieth days of pregnancy. Thereafter it falls to a relatively low level, at which level it remains until about the two hundred and fortieth day, then it rises rather sharply and is maintained at this level until immediately before parturition. The results of MacGregor and Stewart differ from those of Browne, Henry, and Venning (1937), in that the former investigators found a high early level, whereas the latter showed a low early excretion. Browne, Henry, and Venning, however, point out that they were unable to establish the limits of normal variability.

Again, Smith and Smith (1938) studied the metabolism of estrogens in woman. They state that from the time of the second missed period the excretion of estriol is increased at a much more rapid rate than that of estrone, resulting in a higher ratio of estriol to estrone. Preceding delivery the estriol excretion dropped off markedly and there was a concurrent augmentation in the potency of the estrone fraction.

Superimposing the curves of MacGregor and Stewart on our own, both the excretion of the gonadotropic hormones and of pregnandiol correspond very closely with the structural

alterations taking place in the corpus luteum during pregnancy especially at the "critical" period. This paralleling of the biological and morphological findings occurs with such regularity that it cannot be regarded as being fortuitous.

It seems to us that the first 80 days of pregnancy is a "critical" period and is deserving of more intensive investigation than it has hitherto received. If we could at the same time follow histologically the reactions of the human uterus at this period, as Wislocki and Streeter (1938) have done in the *Macaca rhesus*, there is little doubt that we would be in a better position to determine the factors responsible for early implantation and the altered metabolism that takes place in early pregnancy.

#### SUMMARY AND CONCLUSIONS

The gross anatomical and histological features of 13 cases of corpora lutea of intra-uterine pregnancy have been described. Attention is drawn to the importance of examining fresh material, otherwise the very labile cellular inclusions like the lipoid and colloid rapidly disappear after death or after removal from the body.

Corpora lutea removed from patients with ectopic pregnancy, in whom the embryo or fetus is dead, exhibit structural alterations in the contents of the lutein cells and the central cavity.

A curve of the growth of the corpus luteum throughout pregnancy has been constructed. The corpus luteum increases rapidly in size after the fiftieth day of pregnancy. This is maintained until the sixtieth day when it diminishes in size due to the gradual obliteration of the central cavity and a diminution in thickness of the fibrous tissue surrounding the cavity. The lutein tissue remains fairly constant in size throughout the course of pregnancy.

Special attention is drawn to the development of a central cavity containing a potent hormonal fluid.

The theca-lutein cells reach their greatest development at the second to third month and disappear shortly after the obliteration of the central cavity. The granulosa-

lutein cells persist throughout pregnancy.

The two types of cells contain secretory granules, lipid and chromidial substance but the granulosa-lutein cells contain in addition vacuoles and colloid droplets.

Curves of the incidence of lipid secretory granules, and colloid droplets have been constructed. These show that lipoids and secretory granules are most numerous in the early months of pregnancy and diminish toward term whereas the colloid droplets are few in the early months of pregnancy and increase steadily until term.

Chromidial substance diminishes with the progress of pregnancy.

The secretion of the granulosa lutein cells appears as non-stainable secretion in vacuoles which are distributed most abundantly in the cells occupying the inner third of the lutein wall close to the fibrous layer separating the lutein cells from the central cavity. Stagnation of the contents of these vacuoles leads to the formation of the stainable colloid. Colloid is not absolutely specific of pregnancy since 0.75 per cent of the cells contained colloid in a corpus luteum which was removed on the day just preceding the next expected menstruation.

Calcium salt may be deposited in the colloid; this is regarded as a further degeneration of the colloid droplets.

The function of the gravid corpus luteum is re-examined. The accepted viewpoint that the gravid corpus luteum begins to involute only in the second half of pregnancy is called into question and it is suggested that involution may have commenced as early as the second month of pregnancy.

Special attention is drawn to the fiftieth to sixtieth day of pregnancy which we have termed the critical period of pregnancy. At this particular time the corpus luteum undergoes marked structural changes which parallel the metabolic disturbances in the body as indicated by the excretion in the urine of pregnandiol, gonadotropic substances, and the three estrogens—estrone, estradiol, and estriol.

The histological criteria diagnostic of the gravid corpus luteum are shown in the accompanying classification.

# HISTOLOGICAL CRITERIA DIAGNOSTIC OF GRAVID CORPUS LUTEUM

	Early months	Late months
Cavity	Present	Absent
Theca-lutein cells	Present	Absent
Lipoid	Numerous fine droplets occasional cells with large discrete droplets filling cell which may contain cholesterol	Diminished cholesterol containing cells absent
Secretory granules	Numerous	Diminished
Vacuoles	Very numerous	Greatly diminished or absent
Colloid	Present as small occasional droplets in 6 to 5 per cent of cells. Not calculated.	Greatly increased larger and more numerous in each cell. 31 y bc cross calculated

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## REFERENCES

1. AUSTIN, L. B. Developmental Anatomy, 4th ed. Philadelphia, W. B. Saunders Co. 930
2. ARBUTHNOT, L. Lectures on Pathology. New York. Paul B. Hoeber Inc. 924
3. ANDRELL, S. A. Physiol. Rev. 9: 8, 3, 5
4. ANDERSON, M. E. Acta obst. et gynec. Scand. 9: 6, 5. Quoted by Stenman and Robey
5. BRIDGES, A. and HINGHAM, R. 934 Quoted by Stenman and Robey
6. BROUHA, M., and KROCHENKA, L. Bruns-Ber. 934, 4, 712. Quoted by Stenman and Robey
7. BROWNE, J. S. L. HENK, J. S. and V. VON, E. M. J. Clin. Invest. 9: 7, 6, 7
8. BROWNE, J. S. L. and V. VON, E. M. Lancet, 9: 7, 307
9. CARLTON, H. M. Histological technique for normal tissues, morbid changes and the identification of parasites, 4th ed. London Oxford University Press. 938
10. CORNETT, R. M. Irish J. M. Sc. 9: 2, 6 series 530
11. COOPER, G. W. Am. J. Anat., 9: 9, 26, 7
12. IDEM. Am. J. Physiol. 9: 28, 86, 74
13. COUGHER, R. and GROS, G. Compt. rend. Soc. de Biol. Paris, 9: 35, 20, 5
14. DE LEE, J. B. Surg. Gynec. & Obst. 9: 6, 23, 30
15. DONALD, M. Surg. Gynec. & Obst. 9: 3, 5, 5
16. DUFFY, D. Am. J. Anat. 9: 9, 5, 7
17. DUCHESNEAU-ROBINSON, G. and ANDRELL, S. A. J. Physiol. 9: 6, 608
18. E. AND, H. M. KRONA, C. L., and ROBERT, D. H. J. Am. M. Ass. 9: 37, 68, 257
19. FRANKEL, L. Arch. f. Gynaec. 9: 68, 438
20. GILLEN, J. The Golgi apparatus in human (Basal) tissues, its rôle in secretion and its relation to cellular organization. 930. Thesis, University of the Witwatersrand.

- 21 GILLMAN, J, and SMYTH, G S South African J M Sc, 1939, 4 36
- 22 HARRIS, R G Anat Record, 1927, 37 83
- 23 HART, G H, and COLE, H H Am J Physiol, 1934, 109 320
- 24 HARTMAN, C G Am J Obst & Gynec, 1939, 37 287
- 25 HERRICK, E H Anat Record, 1928, 39 193
- 26 JONES, H W, and WEIL, P G J Am M Ass, 1938, 111 519
- 27 KHVATOV, B P Bull de Biol et de Méd Exper USSR, 1938, 5 454
- 28 MACIAS and TORRES 1933 Quoted by Simmonet and Robey
- 29 MARCOTTY, A Arch f Gynaek, 1914, 103 63
- 30 MCGREGOR, T N, and STEWART, C P J Obst & Gynec, 1939, 46 857
- 31 MEYER, R Arch f Gynaek, 1911, 93 354
- 32 MILLER, J W Arch f Gynaek, 1914, 101 568
- 33 MOULONGUET DOLERIS, P Arch d'anat, d'histol et d'embryol, 1925, 4 533
- 34 PARKES, A S J Physiol, 1928, 65 341
- 35 PEUCH and VANVERTS 1913 Quoted by Simmonet and Robey
- 36 PINTO, C Ann di obstet e ginec, 1905, 27 No 2 Quoted by Miller, Marcotty
- 37 PORTES, ASCHHEIM, and ROBEY Gynéc et obst, 1938, 37 200
- 38 PRATT, J P Endocrinology, 1927, 11 195 Quoted by Simmonet and Robey
- 39 RABL, H Anat. Hefte, 1899, 11 111 Quoted by Miller, Marcotty
- 40 ROBSON, J M J Physiol, 1937, 90 145
- 41 SAGLIK, S Contrib to Embryol, Pub 165, Carnegie Inst Washington, 1938, 27 179
- 42 SCHROEDER, R Weibliche Genitalorgane In Handbuch der mikroskopischen Anatomie des Menschen Edited by Moellendorff Vol 7, Part 1 329 Berlin Julius Springer, 1930
- 43 SEITZ, L Arch f Gynaek, 1906, 77 203 Quoted by Miller, Marcotty
- 44 SHAW, W Textbook of Gynæcology London Churchill, 1936
- 45 SIMMONET, H, and ROBEY, M Le corps jaune Paris Masson et Cie, 1939
- 46 SMITH, G VAN S, and SMITH, O W Am J Obst & Gynec, 1938, 36 769
- 47 STEIN, H B South African J M Sc, 1938, 3 102
- 48 VAN DER STRICHT, O Arch de biol, 1912, 27 585
- 49 WALDSTEIN, E Zentralbl f Gynaek, 1929, 53 1305 Quoted by Simmonet and Robey
- 50 WILSON, K M Am J Obst & Gynec, 1937, 34 977
- 51 WISLOCKI, G B, and STREETER, G L Contrib to Embryol, Pub 160, Carnegie Inst Washington, 1938, 27 1

# CARCINOMA OF THE THYROID GLAND

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THE number of proposed methods for classifying malignant disease of the thyroid gland is evidence enough that there is little unanimity of opinion with regard to grouping variations of malignant change in this organ. The published studies also indicate that there are no uniformly accepted criteria for separating definitely benign from early malignant disease in the thyroid gland. Our study has been undertaken to find a means of clarifying this confusion.

The published methods of classifying carcinoma of the thyroid gland vary from a division into scirrhous and medullary types (1) to an arrangement of six groups with several subdivisions (14). Between these extremes many different methods have been suggested for tabulating the variations in malignant disease in this organ (5, 6, 8, 10, 11, 12). Some are based primarily upon the pathological characteristics while others correlate both the clinical and pathological findings. It is our opinion that a satisfactory classification for malignant disease of the thyroid gland must be one that takes into account both clinical and pathological observations.

We have studied 63 cases of thyroid gland disease, clearly malignant or suspected histologically to be so, and we have grouped this material according to several of the proposed classifications. From this comparison of methods for classifying thyroid gland cancer we now feel that the one best suited for general use was suggested by Clute and Warren (3) and it is as follows: Group I (a) Adenoma with blood vessel invasion, (b) Malignant papillary adenocystoma. Group II adenocarcinoma—(a) alveolar adenocarcinoma, and (b) papillary adenocarcinoma. Group III (a) squamous cell

or epidermoid carcinoma, (b) small cell carcinoma, (c) giant cell carcinoma, and (d) fibrosarcoma.

We have tested the practical value of this classification by studying routine sections of cases seen during the last 17 years. Of the 63 cases in which examinations were made 54 were accepted as malignant and 9 were benign as will be made clear later. Many of the cases occurred within the past 5 years but since this is primarily a report dealing with the pathological manifestations of thyroid cancer and their correct interpretation, a study of the tissues from these recent cases has been included. All cases are from the service of Dr. George E. Beilby to whom the authors are indebted for permission to present the material.

The classification of thyroid gland neoplasms is difficult because of the variations in criteria that are employed to differentiate definitely benign from early malignant lesions. Thus, Graham (9) stresses blood vessel invasion while others emphasize the degree of cell anaplasia (12) or invasion of capsule the presence of mitoses (2) or clinically by recurrence or metastasis of the tumor (7) as aids in recognizing malignant change. In the more advanced group II and group III lesions the problem of pathological diagnosis is less serious because there is general unanimity of opinion of their malignant nature. We do not wish to emphasize differences of opinion in the subdivisions of these groups and we have therefore confined our discussion to the development of criteria for recognition of group I tumors. To make certain that we properly interpreted the histological changes for each group in the classification employed, we consulted Dr. Shields Warren who graciously examined all of the sections and made several suggestions.

The method adopted for this study was to examine the routine sections and tabulate in

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TABLE I—CLINICAL COURSE OF PATIENTS IN THIS SERIES

	Operation prior to January 1, 1935						Operation January 1 1935 to March 1 1940						Clinical Diagnosis	
	No Cases	Sex	Alive & well	Dead of carcinoma	Dead other	Recurrence	No Cases	Sex	Alive & well	Dead of carcinoma	Dead other	Recurrence	Benign	Malignant
Group I Malignant adenoma	5	F	3	1	0	0	8	F	7	0	1	0	12	1
Papillary adenocystoma	4	F	1	2	0	0	5	F	3	0	0	2	5	4
Group II Adenocarcinoma	8	F	5	2	1	0	7	6F 1M	2	4	0	1	9	6
Group III Large cell	8	7F 1M	0	8	0	0	4	F	0	4	0	0	1	11
Small cell	4	2F 2M	1	3	0	0	1	M	1	0	0	0	0	5
Totals	29	26F 3M	10	16	1	0	25	23F 2M	13	8	1	3	27	27
Lost	2													

each case a wide variety of pathological changes. Thus for each tumor such facts as variation in tissue architecture, invasion of veins, capsule, or adjacent tissues, and the character of the stroma were recorded. Also enumerated were variations in the cellular morphology, the presence of mitoses, and the degree of anaplasia. These tabulations were studied to learn whether predominance of one or several features could be relied upon to separate benign from malignant lesions. It was found that tumor tissue invasion of veins, capsule, and adjacent tissues constituted the most reliable indications of the presence of malignant disease in the thyroid gland.

In any examination of thyroid gland tissue the first indication of malignant change is departure from normal tissue architecture. Acini are more numerous and compact in some types or show marked papillary formations in others. The presence of solid sheets or cords of cells is an ominous variation from normal. These findings lead to a study of variations in the individual cells, such as abnormalities in the size, shape, staining reactions, and whether or not mitoses can be observed.

If these atypical variations in the tissue architecture and cellular morphology are found to exist, the presence of invasion is the greatest aid in determining whether or not the tumor is malignant. Such invasion, as encountered in routine sections, need not include veins although careful search will usually

demonstrate their involvement in malignant cases. In encapsulated neoplasms, definite evidence of extension of tumor tissue into or through the capsule is as important, in our opinion, as vein invasion. In non-encapsulated growths, invasion of adjacent tissues also carries the implication of malignant change. Care must be exercised to prevent confusing epithelial masses caught in the sclerosis of a benign adenoma with true invasion. The penetration of tumor tissue into at least one of these three structures has been found in each of our malignant cases and a study of additional sections has demonstrated vein invasion in those in which capsular invasion was the first indication of carcinoma.

Endothelium covered masses of tumor cells found within a vessel are regarded as indicative of vascular invasion. It has been possible in some cases to study these masses in serial sections and they have been shown to arise from tumor tissue penetrating the vessel wall. The manner in which the invasion of vessel manifests itself in any given preparation depends upon the plane of the section in relation to the entrance point of tumor into vessel. Thus, in some cases one may see cross-sections of papillary ingrowths which appear to be free in the lumen of the vessel. To avoid mistaking artefacts for true invasion of veins within the substance of a tumor, it is necessary to demonstrate the site of penetration of the vessel wall, however, a large capsular vein

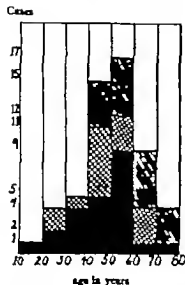


Chart. Age distribution for each group. Black area, Group I, cross hatched areas, Group II, diagonal lined areas, Group III.

filled with tumor tissue should be looked upon as evidence of vascular invasion even though the point of entrance of tumor is not seen.

Figures 1 and 2 indicate types of abnormal appearing thyroid epithelium that may be confused with malignant disease. Nine such tumors have been carefully examined and eliminated from this report because close study revealed that the adenomas did not invade their capsules or surrounding tissues and showed no evidence of invading veins. We direct attention to this group because of the diagnostic problem it presents to the pathologist. Some adenomas so closely resemble malignant tumors that even experienced pathologists differ in their opinions. Figures 3 and 4 illustrate such a tumor. In these borderline cases a study of several sections, preferably serial, in addition to the routine preparations, is necessary before the pathologist can differentiate benign from malignant lesions. To enable the pathologist to give an opinion based upon all significant evidence available a brief clinical abstract should be sent with the specimen. Attention to this detail will give the pathologist a better opportunity to interpret the histological changes and will immeasurably increase the value of his report.

In group I were 22 patients representing 40 per cent of the entire series. It is of interest to note that 2 of the deaths and 3 of the 4 recurrences took place in patients presenting the papillary adenocystoma type of tumor. Two recurrences, one listed as dead of carcinoma in Table I, occurred 5 years after operation. Two other recurrences, one listed as dead of carcinoma in Table I, occurred 3 years after operation. The 4 patients living beyond the 5 year period have survived 9 to 11 years. The patient alive 9 years after our operation had an adenoma of the thyroid gland removed in December 1920. Through the courtesy of Dr. J. L. Donhauser and Dr. J. J. Clemmer of Albany the slide from the original tumor has been made available for our study. We regard the lesion as a malignant adenoma with vein invasion. This patient, therefore, has had a recurrence after 10 years, and by its removal an arrest of the disease for 19 years.

In group I were 13 adenomas with evidence of vein invasion. These arose in so called fetal adenomas and exhibited closely packed acini. Nine tumors were of the papillary adenocystoma type. These were characterized by one or two layers of epithelial cells covering finger like projections of stroma. This histological feature was not always associated with gross cyst formation. The invasive qualities of these two types of tumors, as indicated by their extension into veins, capsule or adjacent tissues, must be demonstrated before they may be included in this group as truly malignant tumors.

There were fifteen patients in Group II, 27 per cent of the series. There were 6 patients who lived 5 or more years although 1 died 6 years after operation from Parkinson's disease and arteriosclerosis (listed as dead of other disease in Table I). Of the 5 remaining 3 have lived 8, 1 has lived 10 and 2 have lived 11 years. These 6 cases represented 75 per cent 5 year cures but the fallacy of small numbers was obvious. Four of the 6 deaths in this group occurred in patients operated upon less than 5 years ago. One of these died after operation.

The adenocarcinomas in group II were either alveolar or papillary in type and exhibited more easily recognized malignant dis-



Fig 1 Benign papillary adenocystoma



Fig 2 Benign adenoma

ease It is at times hard to differentiate between the more malignant cases in group I and true adenocarcinomas A distinguishing feature according to Warren is the presence of broad sheets of anaplastic cells

In this series, group III was represented by 12 cases of large cell carcinoma and 5 cases of small cell type, which together were 31 per cent of our cancer patients We have not seen the squamous cell type One patient has lived for 6 years following her operation and a second patient has survived 3 months Both of these patients had the small cell type of carcinoma and in each the operation consisted of biopsy followed with deep x-ray therapy All



Figs 3 and 4 Borderline malignant adenoma Some experienced pathologists regard this tumor as benign, others consider it malignant





Fig. 5. Recurrent malignant adenoma showing blood vessel and capsule invasion



Fig. 6. Recurrent malignant adenoma growing into blood vessel.

other patients in this group are dead now but lived for an average of 8.3 months after operation, with a maximum of 17 months. One died after operation.

The histological changes of tumors in group III leave no doubt as to the malignant nature of the process, but in certain lesions there is difference of opinion as to whether the tumor is of ectodermal or mesodermal origin. Further investigation is necessary to answer this question.

In this series of cases treatment consisted of excision whenever possible. In clinically inoperable cases a biopsy was taken and deep x ray therapy advised. The fact that this en-

tire series has been treated by one individual adds value to the results obtained.

In group I x ray treatment has been employed in recent cases only: 1 for a recurrence with ultimate death, 2 following excision of a recurrence, and in only 1 case following the primary operation. All others in this Group were subjected to subtotal thyroidectomy with removal of the tumor.

In group II 3 cases, clinically inoperable were treated by deep x ray therapy after biopsy. Two are dead and one still lives with known metastases to bone. A recent case has been treated after the primary removal of the tumor.



Fig. 7. Papillary adenocarcinoma.



Fig. 8. Alveolar adenocarcinoma.



Fig 9 Small cell carcinoma

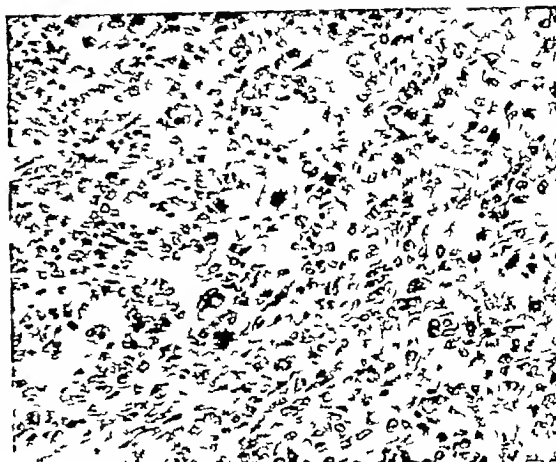


Fig 10 Giant cell carcinoma

Group III cases were nearly all treated prior to the modern, multiple small dose method of roentgen therapy. One patient is alive more than 6 years and received 1,100 r in 6 treatments. All others are dead except one patient operated upon during January, 1940.

We agree with many that surgical removal of the cancerous gland in combination with some form of irradiation offers the patient the greatest hope for permanent arrest of this disease. When the pathological examination reveals malignant change in an adenoma clinically considered benign, the prognosis must be guarded. Because of this uncertain outcome, we can not agree with those (13) who feel that deep x-ray therapy is unnecessary for this type of case.

General considerations of this series as a whole revealed no new features. The age distribution (Chart 1) was in keeping with the published statistics. The sex was of interest only so far as 4 of the 5 males in this series were found to have the most malignant form of thyroid carcinoma. The incidence of cancer in relation to all thyroid operations for the period covered by this study has been 1.5 per cent. In relation to nodular goiters only, the incidence of cancer was 3 per cent. Forty-one of the 54 patients gave a history of goiter for one or more years prior to the time of the operation.

The lack of a standard terminology in the classification of thyroid gland cancer, makes statistical comparisons with the reports of

other authors a dangerous practice, because of the uncertainty of properly interpreting the criteria employed. We have already indicated how we made certain that we understood the criteria for the classification we have used and we can safely say that our study has confirmed the practical value of the classification of Clute and Warren.

We emphasize that this method of grouping thyroid cancer cases conveys definite prognostic information to the clinician. Thus cases in group I, show pathological characteristics that result in low mortality, while the highest death rate is to be expected in cases with the features of group III. We have indicated the

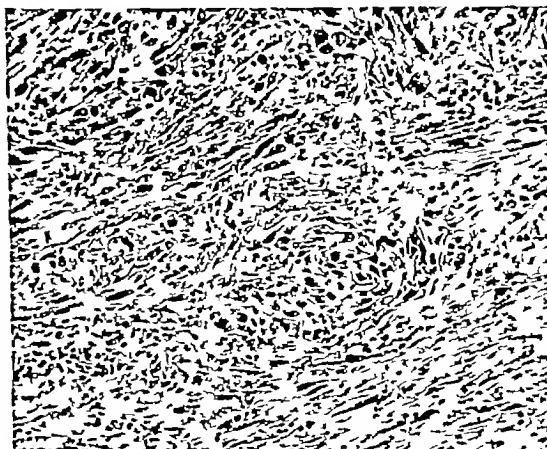


Fig 11 Giant cell carcinoma, spindle form sometimes confused with sarcoma

discrepancies of our small series in comparison with reports of larger numbers of cases (6) in which for example the prognosis in group I is for a 5 year survival in about 80 per cent of the patients. Even with this rather good outlook deaths from these tumors do occur and recurrence of the disease after long intervals may take place. Group II neoplasms are ultimately responsible for death in approximately 66 per cent when a sufficient number of cases are analyzed. The correct diagnosis of a group III tumor carries with it the prognosis of death within a year to all such unfortunate patients with but rare exceptions.

In this presentation attention has been called to the multiplicity of the classifications of thyroid gland carcinoma and the belief is expressed that a lack of uniformly accepted criteria for the pathological diagnosis of malignant disease in this organ may be at least in part responsible for the confusion. It may be due in part to the fact that very few investigators have had an opportunity to study a series sufficiently large to be of statistical value. It is apparent, however, that very little advance toward a solution of the problem of pathological diagnosis of thyroid gland carcinoma has been made since the report of Graham in 1924 when he stressed the importance of blood vessel invasion but also indicated the importance of capsule invasion as a criteria for malignant change. We have not been able to discover any new criteria from the study of this small series but we have indicated the practical value of relying upon evidence of tumor tissue invasion of surrounding structures as encountered in routine sections.

The authors admit the inadequacy of numbers in this study and do not therefore draw specific conclusions. In our opinion it is desirable to plan a method of concerted study that will lead to conclusions which will warrant uniform acceptance. Such a plan would be based upon a collection of all material possible gathered together in one place with statistical interpretation by experienced pathologists.

This plan was presented in detail to the Executive Council of the American Association for the Study of Cancer at its meeting April 29-30, 1930. The Council of the Association approved a resolution to study the problem.

## SUMMARY

1. The classification of thyroid gland cancer is not entirely satisfactory possibly because of the lack of uniformly accepted criteria.

2. Fifty four cases of thyroid gland carcinoma have been analyzed to determine what future studies may help to clarify this confusion.

3. From this analysis it appeared that a statistical study of a large number of tumors collected from all possible sources must be made to assure uniform acceptance of the criteria for and the classification of malignant disease of the thyroid gland.

The authors acknowledge their indebtedness to Dr. Arthur W. Wright for many helpful suggestions during this study.

## REFERENCES

1. BORN, WILLIAM. *The Pathology of Internal Diseases*. 3rd ed., pp. 5-356. Philadelphia: Lea & Febiger, 1920.
2. CLARK, H. M. and SMITH, L. W. Cancer of thyroid gland. *Arch. Surg.*, 1929, 8: 30.
3. CLARK, H. M. and WARRICK, S. Cancer of thyroid gland. *Am. J. Cancer*, 93, 5: 563-583.
4. IDEM. Progress of thyroid cancer. *Surg. Gynec. & Obst.*, 1935, 60: 86-87.
5. COLLIER, F. A. Adenoma and cancer of thyroid, study of their relation to epithelial neoplasms of thyroid. *J. Am. M. Ass.*, 1929, 92: 457-465.
6. COLLIER, F. and COLLIER, G. J. Radical operation for malignant tumors of thyroid gland. *Surg. Gynec. & Obst.*, 1917, 24: 927-934.
7. DEXTER, T. P. Carcinoma of thyroid gland. *Brit. J. Surg.*, 1931, 8: 85-121.
8. FOSTER, J. L. Carcinoma of thyroid. *Surg. Gynec. & Obst.*, 1935, 60: 355-360.
9. GRAHAM, A. Malignant epithelial tumors of thyroid (with special reference to formation of blood vessels). *Surg. Gynec. & Obst.*, 1924, 39: 78-790.
10. IDEM. Malignant thyroid. *Proc. Inter State Post Grad. M. Assoc. N. America*, (1927), 24, 1: 54-56.
11. HARRINGTON, C. D. Cancer of thyroid: its radioactivity. *Am. J. Cancer* (supp.) 93, 5: 1063-1109.
12. PENDERGAST, J. H. Malignant lesions of thyroid gland, review of 774 cases. *T. Internat. Congr. Conf. and Am. Ass. Study of Cancer*, 1935, pp. 51-74.
13. PORTMANN, U. V. Malignant tumors of thyroid gland: report of 300 consecutive cases. *Surg. Gynec. & Obst.*, 1929, 70: 85-100.
14. SMITH, L. W., POOL, E. H. and OLCOTT, C. T. Malignant disease of thyroid gland: clinicopathological analysis of 54 cases of thyroid malignancy. *Am. J. Cancer*, 1934, 30: 51.
15. WARRICK, S. Personal communication.

# THE TRANSPLANTATION OF SKIN AND SUBCUTANEOUS TISSUE TO THE HAND

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THERE are many clear cut indications for transplanting normal covering tissue from one part of the body to another, and in particular from a distant part of the body to the hand. Flame and hot water burns, electrical burns, destruction of covering tissues as a result of severe infection or excessive irradiation, crushing and avulsing injuries, burns due to powerful chemicals all occur with distressing frequency in the practice of every surgeon. To replace the destroyed tissue with normal tissue *at the earliest moment that it can be safely accomplished* is a sound surgical principle. Time, expense for hospital and patient, and, most important, function will be saved if raw surfaces are covered as early as possible with some form of graft or flap.

One cannot forget, however, that, if a patient's vitality is below normal, transplanted tissue heals with difficulty. Long continued suppuration, repeated losses of small amounts of blood, perhaps lack of good food, are all important factors. If a patient's reparative processes are at a standstill a graft, in particular, taken from one part of the body and temporarily deprived of its blood supply cannot be expected to heal over a raw surface. Blood transfusion, sunshine, ultra-violet radiation, vitamin therapy, and good food are all of value in making the patient a better operative risk.

In determining what procedure should be followed in a specific case several general principles should be kept in mind.

1 The fate of the transplant depends upon the development of an adequate blood supply before cellular starvation and resulting necrosis take place. The thinner the graft the more certain it is to survive, simply because there are fewer mouths to feed. The more tissue one attempts to transplant the greater is

the need for nutritive blood serum to maintain life. With each added micron of thickness there is an added hazard that a graft (and by a graft, as distinguished from a flap, is meant tissue which is completely detached from its original blood supply and transferred to a new site) will not survive.

2 In direct contrast with the advantages of the thin graft from the standpoint of certainty of "take" are its disadvantages from the standpoint of functional result. The thinner the graft the less adequately it protects the underlying tissue, the more easily it breaks down when subjected to irritation or trauma, the more certain it is to contract and when laid over a flexor surface to favor development of a flexion contracture. With each added micron of thickness there is added assurance that the graft, if it survives, will give a satisfactory result from the standpoint of function, appearance, and freedom from tendency to contract.

3 Weighing the advantages and disadvantages of grafts of varying thickness it is obvious that the thicker the graft that can be applied with assurance of survival the more satisfactory will be the final result. If the raw surface is successfully covered, however, a graft which is too thin to form an adequate protection can be excised at a later date and a full thickness graft or a pedicled flap substituted for it with every assurance of success, because the newly formed raw surface will be free from infection. If one attempts to transplant too thick a graft and it fails to survive, nothing is gained, valuable time is lost, and the raw surface still remains as an open wound, a potential atrium for further infection, and a site for the formation of the inevitable scar tissue which constantly forms as healing progresses.

4 Certain structures require for their protection and normal function a covering of subcutaneous tissue as well as skin, and we

From the Division of Surgery, Northwestern University Medical School. Read before the Minneapolis Surgical Society, Minneapolis, Minnesota, February 1, 1940.

know of no way of transferring subcutaneous tissue with its covering skin except by the use of a pedunculated flap. Furthermore, these same structures—tendons, nerves, the walls of blood vessels, bones, joint capsules—are so poorly supplied with blood vessels that a graft, as distinguished from a flap laid over them, cannot be expected to survive, simply because there is so little vascular tissue from which new capillaries can develop to provide a blood supply for the newly transplanted tissue.

5 Any one of several complicating factors may add a sufficient handicap to make survival of the transplant impossible. Chief of these is *infection*, and so disastrous is the effect even of a low grade infection that we never attempt to lay a whole thickness graft over a granulating surface or the yellow base left by the excision of exuberant granulation tissue no matter how healthy the granulations appear or how excellent the condition of the patient. Furthermore, only in unusual instances are we willing to lay a flap with an assured blood supply through its pedicle, over a granulating surface, so concerned are we over the destructive effect of even a few bacteria on the vulnerable subcutaneous tissue which forms the undersurface of the flap.

6 The extravasation of only a small amount of serum or blood underneath a graft may form an impassable barrier to the in-

growth of budding capillaries. If every square millimeter of the graft is pressed smooth against the underlying raw surface and held in position with accurately placed sutures and a pressure dressing, such extravasation is unlikely to occur and the most favorable conditions for rapid formation of the new capillary network are afforded. No one has emphasized these facts more persistently and effectively than Blair Brown and their associates and no one has described so well the various methods available for maintaining pressure over a graft or demonstrated so conclusively its importance in securing good results.

7 It is to Blair and Brown too that we are indebted for constant emphasis on the importance of clean cut excision of redundant granulations so as to provide a smooth yellow base over which to apply a graft of intermediate thickness. If an infected wound has been dressed with scrupulous clean care from day to day and with the constant application of sponge pressure outside the sterile dressing, the granulations may become so firm and healthy that no excision of granulation tissue is necessary. Frequently however some exuberant growth and congestion develop, and a soft congested, granulating surface, which projects above the level of the surrounding skin, does not form a favorable base upon which to lay a graft.

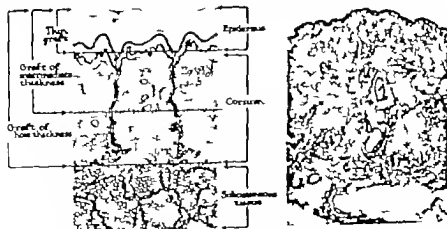


Fig. 1 Diagram showing skin in cross section, and thickness of skin included in different types of graft. 1 the photomicrograph of similar section of skin, at the right, can be seen the numerous epithelial elements which the

corium—hair follicle, sebaceous and sweat glands, from which the epidermis is rapidly reformed, even though the entire epidermis and part of the corium has been removed for use as graft.

For the great majority of cases with a surface defect of the hand we have come to depend upon one of three types of transplant the graft of intermediate thickness, the graft of whole thickness skin, and the pedunculated flap (Fig 1). Rarely the thin graft with little derma and the pinch grafts of Reverdin or the thicker grafts of Davis offer advantages over the graft of intermediate thickness.

#### THE GRAFT OF INTERMEDIATE THICKNESS

The indications for the use of this type of graft and the technique of its application have been presented in such comprehensive fashion by Blair and Brown in a classical paper in *SURGERY, GYNECOLOGY AND OBSTETRICS*<sup>1</sup> and in a more recent paper by Brown in the *Annals of Surgery*<sup>2</sup> that it would be both presumptuous and wasteful of printer's ink to discuss the subject at length. In covering raw surfaces on the hand the graft of intermediate thickness has a wide field of usefulness. It can be laid over a clean granulating surface or over the yellow base left by the excision of redundant granulation tissue. In other words, it can be used advantageously for the patient who has suffered an extensive burn, a crushing or avulsion injury, or an infection with loss of tissue as soon as the raw surface

is clean and the patient's general condition permits (Figs 2, 3). It can be used to cover freshly made raw surfaces, *if the patient is seen within a few hours* of the time of injury, and if there is still subcutaneous tissue present in the floor of the wound to provide a source of blood supply and to protect the important deeper structures—tendons, nerves, and blood vessels. An often neglected opportunity for the application of such a graft, as emphasized by Reed and Harcourt, is after traumatic amputation of a finger tip (Fig 4) crushed between a door and its frame or caught in a punch press.

Because such a graft can survive, even if there has been some impairment of blood supply of the surface over which it is laid, it is often possible to apply a graft of intermediate thickness immediately after excision of skin damaged by excessive irradiation, if sufficient time has been spent before operation to control the infection which is invariably present on the surface and in the deeper layers of the skin (Fig 5). Even if a part of the graft fails to survive, complete healing can usually be secured by careful and cleanly after-care and, if necessary, a second graft can be laid over small raw surfaces that fail to show rapid tendency to heal from ingrowth of adjacent epithelium.

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Fig 2 Flame burns of both hands first seen 3 weeks after injury. Grafts of intermediate thickness were applied after 9 days of treatment to overcome infection.



Fig. 3. Result of application of grafts of intermediate thickness for flame burns of forearm.

In preparing a raw surface for application of the graft we have come to rely on cleanly surgical care of the open wound, the constant application of moderate pressure over the raw surface, and rest with the aid of light aluminum splints. In dressing the wound every effort is made to avoid constant tearing down of healing tissue by rough treatment and abrupt tearing away of dressings. The raw surface is cleansed by irrigation with salt solution and gentle sponging. Tissue which is obviously necrotic is cut away without cutting into healthy granulations. The area about the wound is kept clean and free from crusts and epithelial debris by soap and water cleansing. In dressing the wound at least one layer of very fine meshed gauze, such as old handkerchief linen or very fine meshed muslin, is laid directly over the raw surface. Fine meshed

gauze does not readily permit growth of granulation tissue into its interstices. If the newly formed tissue does not adhere to the overlying dressings it is not repeatedly traumatized and broken down as the dressings are changed.

The fine meshed gauze over the wound and a few additional layers of flat gauze are moistened with sterile boric or salt solution so as to provide a moist dressing and favor drainage of wound secretion into the dressings. Oil dressings and dry dressings favor retention of wound secretion and the formation of small accumulations of pus which act as culture tubes for the rapid growth of any bacteria present.

Over the moist dressings are laid dry sterile dressings in sufficient thickness to permit absorption of all wound secretion. Over the dry dressings are bandaged clean soft marine



Fig. 4. Result of application of graft of intermediate thickness 43 hours after partial amputation of tip of ring finger. (Patient, as first seen, 3 days after injury.)

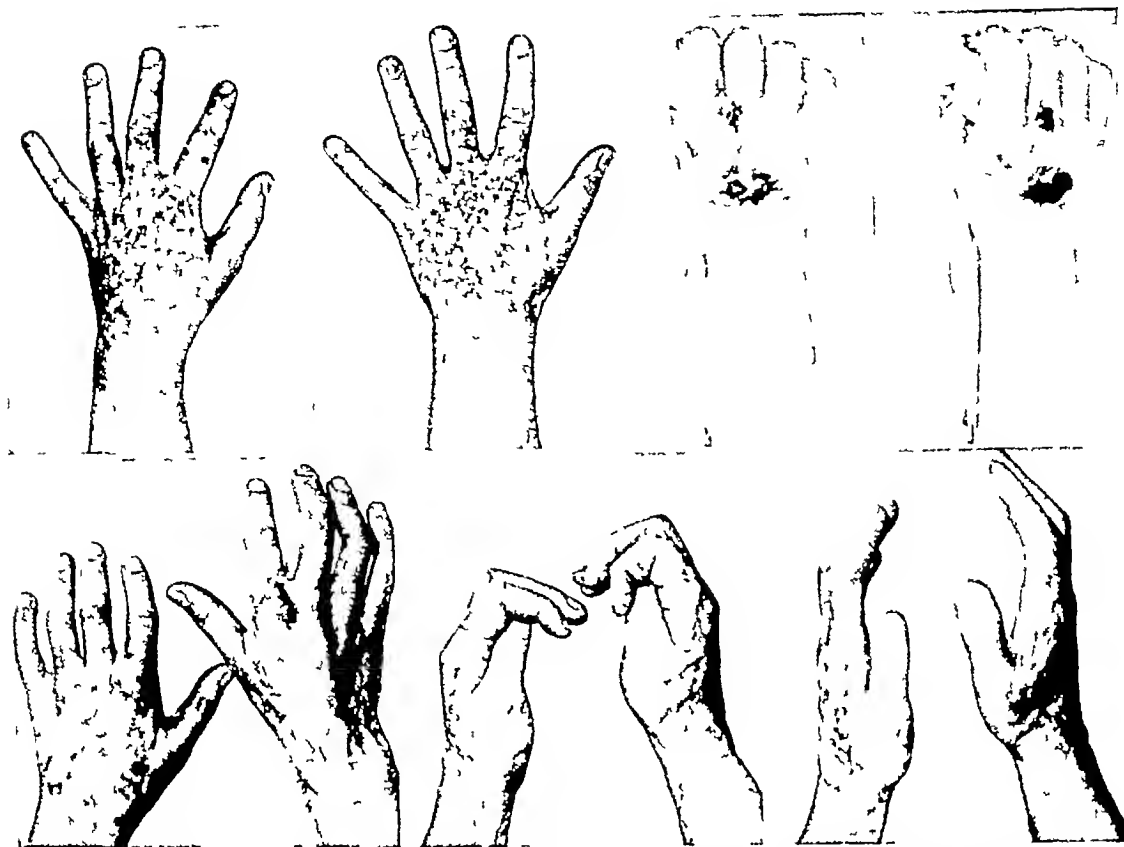


Fig 5 Result of application of grafts of intermediate thickness for irradiation dermatitis and ulceration develop-

ing over a period of 9 years Result 8 months after operation on right hand, 4 months after operation on left.

sponges in sufficient number and with sufficient pressure to provide a moderate pressure over the entire wound surface. The bandaged hand is immobilized in a light splint, and in such a position as to favor function. If the raw surface involves the dorsum of the hand the fingers are bandaged in semiflexion, if the palm is affected, in extension.

It may surprise the skeptical individual to learn how quickly a "dirty" hand with an extensive wound partially covered with sloughing skin, with dried crusts and with fragments of tissue coagulated by tannic acid can be converted into one suitable for the application of a graft by simple cleanly treatment, the application of pressure over the dressing and continuous rest obtained with the aid of a splint.

At the time of operation the donor site is prepared with plain white soap and water and

without antiseptics. We believe it is good technique to secure the graft as soon as the donor site is prepared and the field draped, to fold it in moist gauze so that only the epithelial surface is exposed, to apply a smooth snug pressure dressing over the donor site with a few thicknesses of fine meshed gauze saturated with petrolatum next to the raw surface, and, while the surgeon stands aside, to have one member of the team remove the dressing from the hand and irrigate the area to be covered with warm salt solution. If the dressings have been carefully done in the days before the operation little cleansing of the hand should be necessary in the operating room. The more rapidly the graft can be applied to the raw surface after the pressure dressing is removed, the less opportunity is there for congestion of granulation tissue to develop. We have sometimes seen large raw



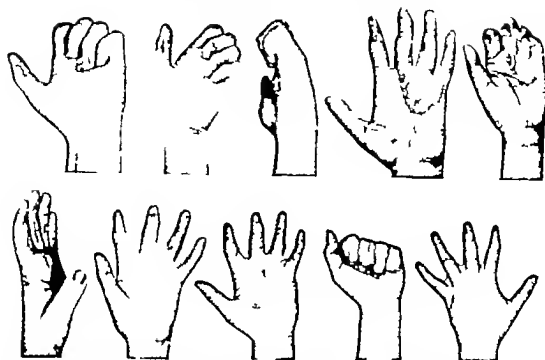


Fig. 6. Mergle burn resulting in destruction of palmar skin to very tips of fingers. Immediate result and result

six months after application of grafts of whole thickness skin, and of small flap to distal palmar of index finger.

surfaces which appeared red and firm immediately after the pressure dressing was removed became dusky and congested while the surgeon was cutting grafts with which to cover them. If firm red granulations cover the open wound and the raw surface forms a slight concavity instead of projecting above the level of the adjacent skin edges, the graft is laid directly over it without further preparation. If excessive granulation tissue is present it is shaved away as smoothly as possible.

It is advantageous to cover the raw surface with a single graft which projects a little beyond the margins of the raw surface. Time is lost and the operation becomes much more difficult if several grafts must be applied and anchored in place. To secure a graft of adequate size the suction boxes and long thin knives devised by Blair are very helpful. The device of Padgett and Hood for holding the skin taut and securing a graft of uniform thickness makes a simple procedure of what otherwise calls for skill and long experience.

The importance of anchoring the graft securely and under tension, of providing a few openings for escape of serum from underneath it, and of applying the dressing in such a way that every square millimeter is firmly apposed to the underlying surface has been frequently stressed by Blair and Brown and these details are of importance in assuring success.

At times, particularly if we are uncertain as to whether infection is completely under control tubes of the Carrel type are incorporated in the dressing so that it can be kept moist by 4 or 6 hourly injections with salt solution without disturbing the dressing or releasing the pressure. The open ends of the tubes are protected with sterile gauze, and the nurses in charge are carefully instructed concerning the importance of not adding contaminating organisms by careless technique in the injection of the solution.

If the graft has been laid over a granulating surface or over the raw surface left by excision of irradiated skin the primary dressing

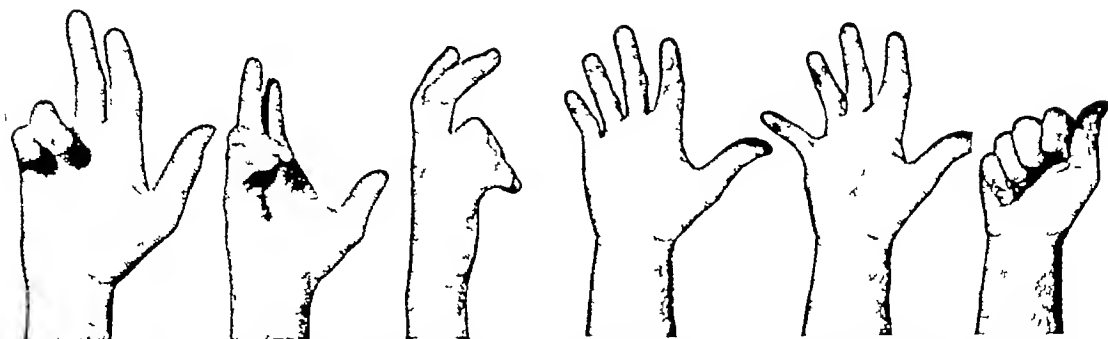


Fig 7 Contracture following a burn sustained at age of 3 years, operated upon unsuccessfully 4 years and 8 years

afterward Appearance of hand at age of 23 years and result after application of graft of whole thickness

is left undisturbed for 4 or 5 days, and for as long as 8 days if the graft has been laid over a recent wound and if no symptoms of developing infection—fever, redness and swelling above the involved area, throbbing and pain—have appeared

The first dressing is removed with every care to avoid tearing away healing epithelium. Sutures are removed, and any redundant portions of the graft are cut away. If the graft is pink and dry a simple dry dressing or a petrolatum gauze dressing is reapplied and pressure is maintained over the wound for another 4 or 5 days. If any small pools of pus or wound secretion are present they are wiped away with sterile applicators and the same type of moist dressing is applied that was used during the pre-operative period. The dressing is then changed once daily, and the pressure and splinting are maintained until healing is complete and every square millimeter of raw surface covered with epithelium.

If loss of a portion of the graft 15 centimeters, or more, in diameter takes place a second graft is applied as soon as necrotic tissue has separated and the raw surface is again red and healthy. Though this may not often be necessary it is just as logical not to wait for spontaneous healing of such a raw surface as it was in the case of the original wound.

A word should be added concerning the pinch graft or small deep graft. To us it has seemed that there are few indications for their use. It has been our misfortune to have seen rather frequently the site of an extensive burn or avulsion injury covered with uneven, pock-marked epithelium, and to have been often confronted with patients with large raw surfaces still uncovered in whom practically every available donor site has been converted into irregular areas unsuitable for use as the source of a graft of intermediate thickness. Today the use of the Reverdin graft frequently seems a makeshift substitute for a good

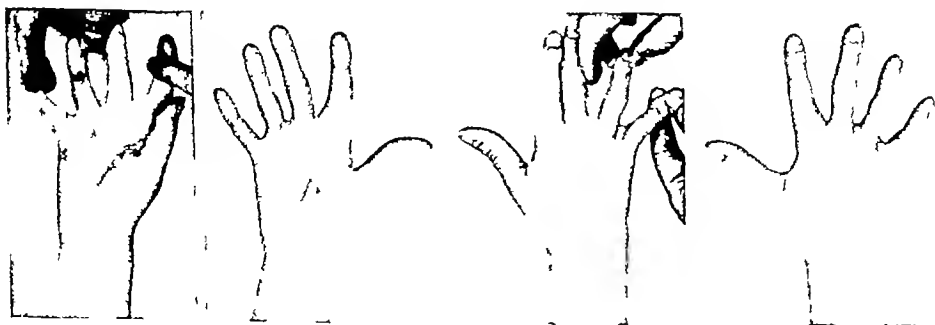


Fig 8 Result of application of graft of whole thickness skin for burn contracture of palm, and of similar grafts to overcome residual syndactylism.

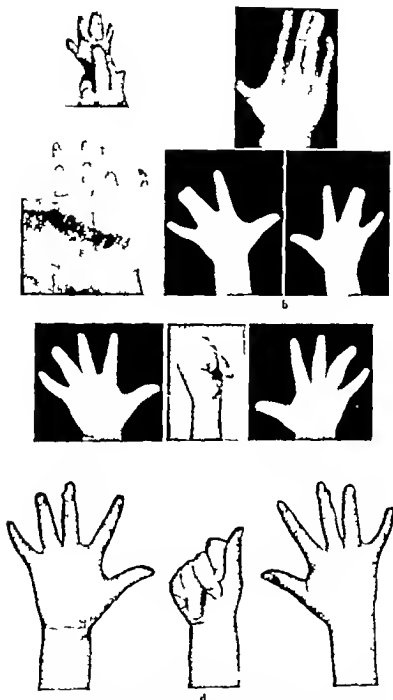


Fig 9. Syndactyly of middle and ring fingers. a, Appearance 1 year b, 4 years c, Result immediately after operation and d, 5 years later

surgical job We would use it only in patients unable to take an anesthetic and in whom there might be some advantage in planting a few islands of epithelium in the middle of a raw surface, and in patients with an anaerobic streptococcic infection, such as Meleney has described, in whom there would be a definite risk in covering the entire raw surface at one time and applying over it an occlusive dressing

#### THE GRAFT OF WHOLE THICKNESS SKIN

The indications for the use of this graft and the technique of its application have been very fully and clearly presented by a number of American surgeons—notably by Blair and J S Davis, more recently by Garlock, Dragstedt and Wilson, MacCollum, Conway and by Dufourmentel and Tierny of France

In surgical conditions involving the hand we have found the graft of whole thickness skin of particular value in the treatment of contractures resulting from burns, in the treatment of syndactylism, of Dupuytren's contraction, of irradiation dermatitis without ulceration, and occasionally in the immediate repair of wounds following crushing or avulsion injuries

*Burn contractures* Rarely does one encounter such thick keloid-like scar tissue as forms over the palmar surface of hand and fingers following a deep burn, and particularly so if during the process of healing efforts have been made to keep the fingers extended by some form of tension splint Fortunately for patient and surgeon the tough and resistant palmar and digital fascia acts as a barrier to protect the deeper lying tendons and nerves, so that in most instances of burns of the palmar surface one can still find after complete excision of the dense covering scar a thin layer of fairly normal connective tissue covering tendon sheaths, nerves, and blood vessels In such a case the graft of whole thickness forms the simplest and most satisfactory method of covering the raw surface (Fig 6) Its advantages are many the operation, though tedious can be completed in one stage, the graft is accurately sutured to the free margin of the defect so that the wound is closed and postoperative care is reduced to a minimum,

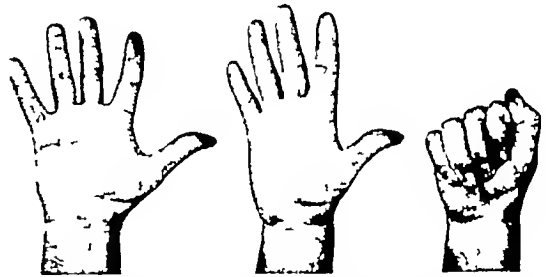
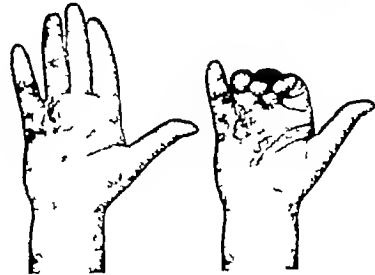
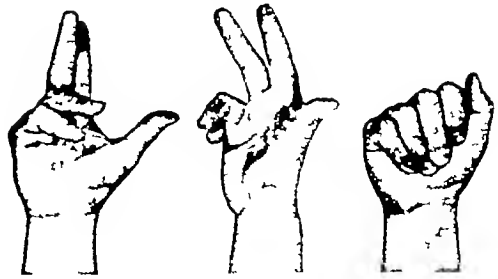


Fig 10 Result obtained in case of long standing Dupuytren's contraction after excision of contracted palmar fascia and application of graft of whole thickness to replace defect over ulnar side of palm and between little and ring fingers

the graft can be made to conform to a raw surface of irregular outline and curving base—an important advantage which this graft possesses, as compared with the pedunculated flap, when the web between the fingers is involved and the deforming scar has bound the fingers in an acquired syndactylism (Fig 7)

As complete excision of contracting scar tissue as it is possible to accomplish is essential for success This often means a long and tedious dissection and always constant care to avoid tangential injury of digital nerves and blood vessels, often drawn out of their normal position by contracting fibrous tissue If during the progress of the dissection one constantly holds taut the dense scar tissue as

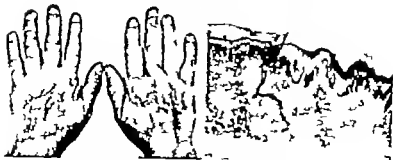


Fig. Application of grafts of whole thickness skin over proximal phalanges of left middle and ring fingers for irradiation dermatitis

It is cut away from the underlying surface it is easy to cut away a section of a digital nerve under the impression that one is excising only the greatly thickened covering tissue. A bloodless field, secured with the aid of a blood pressure cuff inflated to 260 millimeters pressure and repeated relaxation of the tension with which the excised tissue is drawn away from the raw surface as it widens during the progress of the dissection help the surgeon to avoid such injury.

In severe flexion contraction of the fingers our greatest difficulty has usually been to excise completely the scar tissue at the sides of the fingers, where the volar digital fascia becomes continuous with the fibrous expansion of the extensor tendon. Here, too, the digital nerves and blood vessels are usually intimately fused with the contracting scar and the danger of injuring them is especially great. As the dissection is continued and fingers long contracted are gradually drawn into extension the contracted digital nerves and blood vessels may begin to stand out as taut bow strings. In cases of long standing contracture it requires great care to avoid rupture of these taut slender structures and to provide for them some protective covering of soft tissue.

One can hardly overemphasize the importance of excising the contracting scar so completely that the remaining normal tissues are permitted to retract to their normal position, and so that normal tissue to which the graft can be sutured is present at the margin of the defect. If scar tissue is left behind some contraction of the suture line and partial recurrence of the contracture particularly in a

growing child, are certain to result. Scar tissue at the margin of the defect also interferes with vascularization of the graft, and the development of a blood supply from the skin margin is an important factor in the healing process.

An exception to this rule of complete excision of scar tissue is made in cases in which such extensive keloidal thickening has developed as a result of constant and repeated tension that complete excision would be inadvisable because of the extent of involvement or because of the patient's physical condition or youth. With thick keloidal masses on the dorsum of the hand for example which prevent separation of the fingers from one another but which do not extend to the palmar surface we have seen excellent results, and remarkable flattening of the thick scar tissue left behind after simple longitudinal di-



Fig.

vision of the keloidal tissue at the clefts between adjacent fingers so as to permit separation of the fingers without tension, and the application of whole thickness grafts over the normal subcutaneous tissue exposed in the "valleys" between the "walls" of scar tissue. Similarly, good results have been secured simply by dividing thick contracting cords over the dorsum of the wrist or over the flexor surface of the elbow and covering with a whole thickness graft the considerable raw surface exposed by the wide retraction of the tissues released from tension.

**Syndactylism** The plastic procedures suggested by Zeller, Dieffenbach, Felzetz, Didot, Faniel, Rudulesco and others for the care of syndactylism are to us of historical interest only. They appear simple and adequate as described in textbooks of surgery, but we have never seen a successful result from the attempt to make the tissue present on the hand suffice for covering the raw surfaces resulting from surgical separation of completely fused fingers. On the contrary we have seen deformities and contractures with both flexion and lateral deviation, deformities exceedingly difficult to correct, result from the attempt to treat syndactylism by one of these various procedures.

The explanation is simple. When the fingers are separated sufficiently to permit normal abduction there is simply not sufficient tissue

available to cover the raw surface. The greatest deficiency, moreover, is at the base of the cleft between the adjacent fingers—the site at which scar formation is certain to produce recurrence of syndactylism. Unless one faces the simple fact that no good result can be obtained by attempting to stretch an insufficient supply of covering tissue over an extensive raw surface, failure is certain to result. Moreover, the necrosis that results from excessive tension along the suture line and the inevitable infection that follows separation of skin edges as sutures cut through them, produce scars that gradually draw the affected fingers into an awkward position and that are exceedingly difficult to remove and counteract at any secondary operation.

Any operation for syndactylism should be postponed until the period of rapid growth is past, unless fingers are being drawn into a lateral deformity by the fusion with adjacent fingers. No matter how deeply the cut is made to separate the fused fingers and how carefully the graft is applied, if the patient is operated upon during the first few years of life, recurrence of the deformity is almost certain to take place because the transplanted tissue does not keep pace in growth with the rapidly growing hand. We would prefer never to operate upon a patient before the age of 4 or 5 years (Fig. 9), and would wait until the age of 10 or 11 if there were no indication of in-

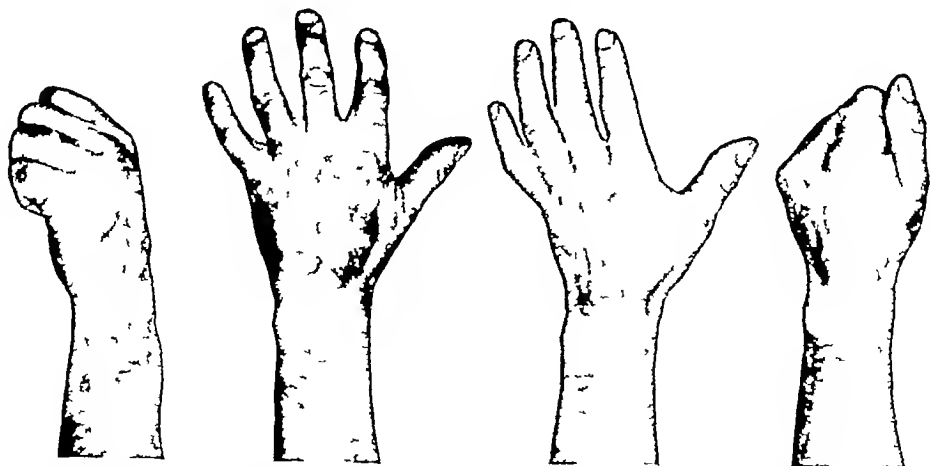


Fig. 12 Result of immediate application of grafts of whole thickness skin to fill defects resulting from crushing injury (Appearance of hand after injury is shown on opposite page.)

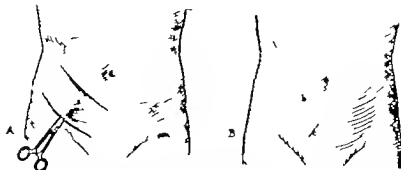


Fig. 3. Diagram illustrating method of raising delayed flap. Flap is cut across at lower end, after incisions *a* and *b* are beveled.

creasing deformity. When recurrence and contracture have developed following an operation performed in infancy secondary operation is made difficult by the presence of scar tissue and sometimes precarious because of injury of tiny digital blood vessels at the primary operation.

When operation is carried out the separation of the fingers should be carried as deeply as possible without injuring the digital vessels and digital nerves as they separate in Y shaped fashion to pass to the sides of the adjacent fingers. The separation should be carried farther proximalward on the dorsal than on the palmar surface as Kanavel emphasized in his scholarly monograph on "Congenital Malformations of the Hand" the floor of the web slopes proximalward from palm to dorsum and this obliquity should be kept in mind in separating the fingers and in cutting the graft.

In cases in which the skin is lax or somewhat redundant at the level of the web and in which some subcutaneous separation of the fused fingers is possible we frequently use the relaxed skin and most of its subcutaneous tissue as a pedunculated flap with its base on the dorsum of the hand to cover the base of the cleft between the fingers after they have been separated. Two single grafts of whole thickness skin are then applied to cover the remaining raw surfaces on the opposing sides of the separated fingers. The more complete and close the fusion between adjacent fingers the more inclined we are to use the single graft as described to cover the entire raw surface.

*Dupuytren's contraction.* Failure to secure a good result in patients with Dupuytren's contraction is just as certain to result from the attempt to stretch contracted skin over an extensive raw surface as from failure to carry out complete removal of the thickened and contracted palmar and digital fascia. Even in cases in which the skin is not contracted it may be so intimately fused with the thickened fascia underneath that its vitality is impaired, and if undermined skin is left behind in the hope of avoiding the use of a graft dry necrosis and separation eventually take place with long delay in healing scar formation, and tendency to recurrence of the deformity.

The use of a whole thickness graft is the simplest and most satisfactory method we have found of replacing hopelessly involved skin, and of making it possible to close the wound without excessive tension when the fingers are again permitted to come into extension as a result of the removal of the thickened and contracted fascia. We have not often secured complete and primary healing of such grafts, but have not failed to secure eventual healing and a good result by cleanly surgical care of the grafted area and maintenance of a pressure dressing until healing was complete (Fig. 10).

*Irradiation dermatitis.* If in an area subjected to excessive irradiation multiple keratoses have developed and so close to one another that excision and suture cannot be carried out, the excision of the affected area and its replacement by a whole thickness graft affords a simple solution of the difficulty.

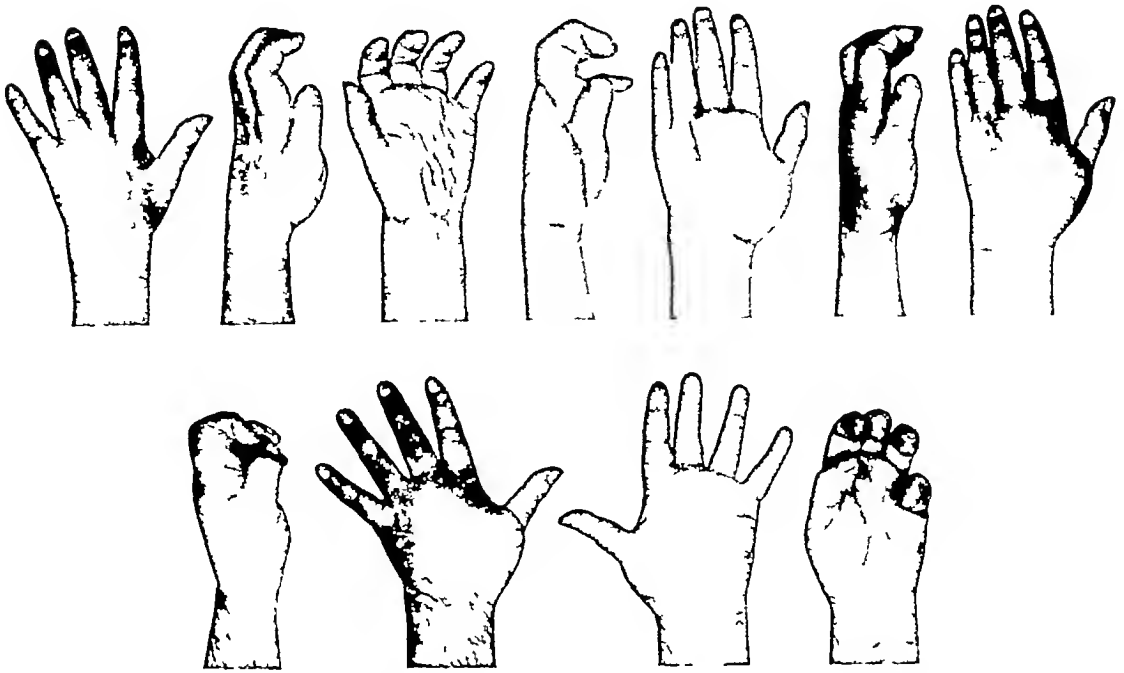


Fig 14 Crushing injury of left hand, with intermediate and late result of application of pedunculated flap

If skin over the dorsum of a phalanx is excised and the defect covered with a whole thickness graft from the inner surface of the arm healing can take place so rapidly and perfectly that 6 months later it will be difficult to determine on which finger the graft has been laid (Fig 11)

If ulceration has already begun we would rarely attempt to use a whole thickness graft but would apply one of intermediate thickness after infection had been controlled as completely as possible by simple cleanly surgical care, immobilization, and pressure dressings

*Recent injuries* If a patient is seen within a few minutes or few hours after sustaining a lacerated wound or avulsion injury with loss of covering tissue, or a crushing injury with destruction of the superficial tissues, and if the patient's condition is such that an immediate cleansing and repair of the wound can be carried out, there is every reason for converting the contaminated wound into a clean wound and closing the wound. These seem to us primary principles of surgical care which are accepted by thoughtful surgeons everywhere

To cover the raw surface in such a case the application of a whole thickness graft may give the best result attainable (Fig 12). Obviously one must have a source from which to obtain a graft of suitable size, a raw surface with adequate blood supply, and with sufficient soft tissue still present to afford protection for underlying nerves, tendons, blood vessels, bones, and joints. Under such conditions the graft of whole thickness skin possesses the same advantages that were cited in the paragraphs under "Burn Contractures"

#### THE PEDUNCULATED FLAP

When structures are laid bare which require for their protection and functional activity a covering of subcutaneous tissue as well as epithelium—structures such as tendons, the larger nerves, and blood vessels—or if the loss is still greater and bones and joints are exposed, the use of a pedunculated flap is imperative. We know of no way of transferring subcutaneous tissue with its overlying skin from one part of the body to another except by maintaining a part of its original



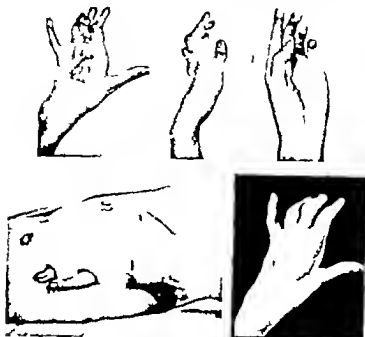


Fig. 5. Mangle burn. 1st, result of application of pocket flap and subsequent separation of fingers. 2nd, aid of skin thickness grafts.

blood supply while new vascular channels be-  
tween the base and the transplanted tissue  
are being formed. To cover such raw surfaces  
on the hand we have come to depend upon  
two types of flap—the *delayed flap* from  
the anterior abdominal wall or anterior sur-  
face of the thigh, and the *'pocket flap'* from the  
same sites. In speaking of a delayed flap we  
refer to the flap which is prepared for transfer  
by raising it in one or two stages and which  
after it is raised, is immediately returned to its  
original site and sutured in place (Fig. 13).  
By permitting a flap to remain at its original  
site for two or three weeks, as Blair pointed  
out many years ago in his paper on the de-  
layed transfer of long pedicle flaps, the blood  
supply entering the flap through its pedicle is  
stimulated and increased to such an extent  
that it is possible eventually to incise a fairly  
long flap along three sides and transfer it to  
a new site without loss of any portion of the  
flap. The term *'pocket flap'* is self-explanatory  
but even with this type of flap we prefer  
if possible to raise a part of the flap and re-  
turn it to its original site for a period of 12 or

14 days rather than to raise the flap and place  
the hand underneath it at the primary oper-  
ation.

The use of the delayed pedunculated flap  
has many advantages. The flap can be raised  
under local anesthesia. One can carry the  
separation of the flap as far as seems advisable  
and stop short if there is evidence that further  
elevation at the primary operation would  
jeopardize its vitality. One can cut the flap  
of the desired thickness, an important point  
when one is attempting to secure an extensive  
thin flap to replace the thin layer of skin and  
subcutaneous tissue that covers the tendons on  
the dorsum of the hand. Most important of  
all, when the flap is ready for transfer one  
can incise it along three sides, raise the flap  
from its bed, cover the raw surface under-  
neath it with a graft of intermediate thickness  
or by drawing the edges of the defect together  
with sutures, and attach the flap along prac-  
tically its entire free border to the edge of the  
defect on the hand. Such a procedure makes  
the operation almost a closed one for the  
only exposed raw surface is the under surface

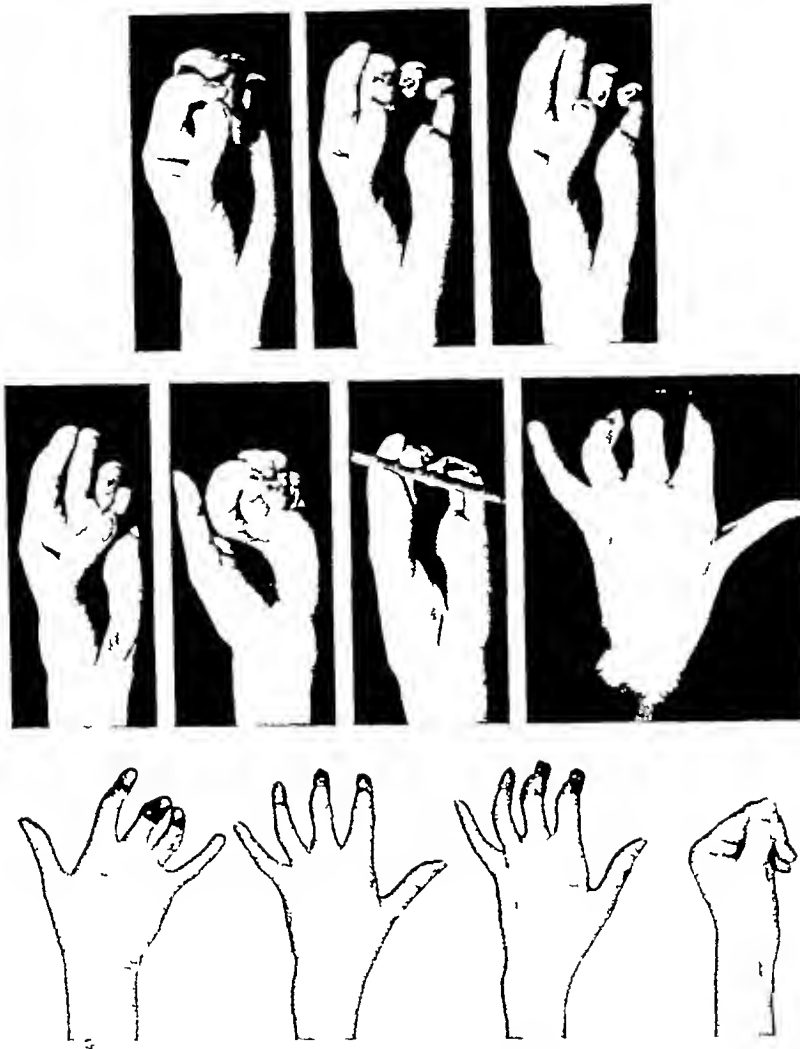


Fig 16 (Legend on opposite page )

of the pedicle as it passes from abdomen or thigh to hand. We have frequently seen such flaps heal by primary union to the edges of the defect on the hand, and with so little inflammatory reaction about the pedicle of the flap that only occasional dressings were required during the 3-week period that is ordinarily allowed for development of the new blood supply to the flap.

Because the pocket flap has a double pedicle and often additional small pedicles between the fingers it can be raised and laid over the raw surface at the primary operation

without running serious risk of loss of a part of the flap. Because, however, there is an extensive raw surface exposed to intimate contact with skin surface, where the palm rests on the raw surface underneath the flap, some inflammatory reaction is inevitable, considerable wound discharge results, and when the flap is separated from its attachments to abdomen or thigh a considerable raw surface is left which must still be covered with grafts of intermediate thickness.

In passing, we have not been able to secure healing of the raw surface underneath a pock-

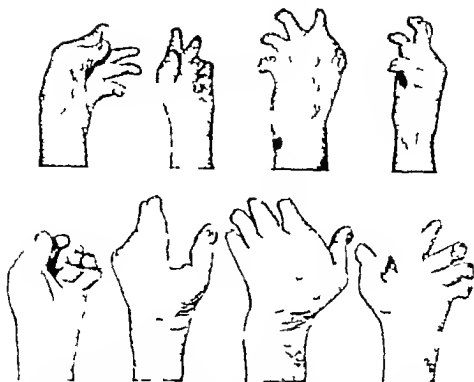


Fig. 6. Complete loss of function of hand following flame burn. Result of application of large pedunculated flap surrounding hand and separating thumb from hand.

et flap by attaching thin grafts, raw surface outward to the palm before placing the hand underneath such a flap. When this has been attempted the grafts have simply melted away and no epithelium has remained attached to the raw surface when the pedicles of the flap were divided and the hand lifted away. Furthermore since we have limited the surgical preparation of the hand to careful and prolonged soap and water cleansing and have applied no antiseptics to it before it was placed underneath the flap there has been a marked diminution in the amount of wound secretion developing underneath the hand. As a result the care of the wound area has been simplified and preparation of the raw surface for grafting after the hand has been lifted away from the raw surface has required a week or even less, instead of 12 or 14 days.

The chief indications for the use of pedunculated flaps in our experience have been to cover the dorsum of the hand after deep and

extensive flame or electrical burns or after injuries in a hot mangle to secure a covering of normal skin and subcutaneous tissue over the defect left by separating the thumb from the hand and to replace the covering tissue of hand and forearm after severe infection or crushing injury. Occasionally such flaps have been used after deep chemical burns, after crushing injuries with loss of part of one or more fingers, after removal of a tumor or after extensive removal of tissue devitalized by excessive radiation. In earlier years a number of cases of burn contracture of the palm were treated by laying the hand underneath a double pedunculated flap taken from the lumbar region. After Blair had demonstrated the possibility of securing more satisfactory results by the simpler method of employing grafts of whole thickness skin, pedunculated flaps have been used rarely for such cases and only in cases with some unusual complication.

*Deep burns of the dorsum of the hand* (Figs 14, 15, 16) There is no more difficult problem in connection with the surgery of the hand than restoration of usefulness in a hand in which covering tissues, extensor tendons, periosteum, and dorsal joint capsules have been destroyed more or less completely as the result of a deep burn and the infection which has invariably followed it. A discussion of this entire problem would lead one far beyond the subject of our paper, but it is obvious that the first step toward restoration of function is replacement with normal tissue of the shiny, tense tissue paper-like epithelium which nature left to itself provides as a covering for an extensive raw surface. A satisfactory covering must be flexible so as to permit free movement at the metacarpophalangeal and interphalangeal joints, it must be free from a tendency to contract, and it must be of such a thickness that tendons can be transplanted underneath it at a later date. It is obvious that it would be impossible to transplant tendons underneath a graft of intermediate thickness or a whole thickness graft, even if it were possible to secure healing of such a graft over the deeply denuded dorsum of the hand, yet a visiting surgeon from abroad wrote somewhat disparagingly of the appearance of the pedunculated flaps of some of our patients, as compared with grafts. The fact that these flaps were to serve later both to protect tendon transplants and to make possible their gliding movement had escaped him completely.

In preparing the usual delayed flap for transplantation to the dorsum of the hand it is our custom first to outline the flap by parallel incisions, made if possible parallel to the course of nerves and major blood vessels (Fig 13). The skin and desired thickness of subcutaneous tissue over the entire area outlined by the parallel incisions are raised at the first operation. All bleeding vessels are ligated with fine silk ligatures, and the flap is sutured with care not to crush or devitalize skin edges.

At the end of 10 days the distal end of the flap is cut across, and at the end of another 10 days it should be possible to incise the flap along the healed incisions, divide the subcutaneous tissue at the proper depth to give the desired thickness, and transfer the flap

to its new site. Before the flap is actually spread out over the raw surface it is intended to cover, the edges of the defect left by elevation of the flap are approximated with sutures, or, if approximation would produce excessive tension the edges of the defect are drawn inward so as to make the raw surface as small as possible and the remaining raw surface is covered with a graft of intermediate thickness. The hand is then brought underneath the flap and the flap sutured in place over the freshly prepared raw surface.

If the flap is of such size and shape that a relatively narrow pedicle remains as the sole source of blood supply, this pedicle is usually divided completely at the end of 3 weeks and suture of the flap to the hand is completed.

If instead of the type of flap described a pocket flap has been used it may be wise not to detach the entire flap from its original site at one stage. In such cases we have often divided the flap along one side of the hand,—the lower pedicle of an abdominal flap, for example, or the lateral pedicle of a thigh flap—sutured the freed edge of the flap to the hand, and waited for another 8 or 10 days before dividing the remaining attachments.

As indicated above one of the most difficult problems in the reparative treatment of deep burns of the dorsum of the hand is to secure sufficient tissue for restoration of the web. Because of the tendency of the scarred fingers to remain fixed in close adduction it is difficult to hold them abducted underneath a pocket flap and so secure tissue which can eventually be turned down between the fingers to restore the web. We have sometimes met this problem by the use of whole thickness grafts between the fingers after the flap was well healed, as described in the treatment of syndactylism (Fig 15). Pierce and O'Connor have suggested dividing the distal portion of the flap into strips for the individual fingers and suturing the strips to the fingers at the time the hand is laid underneath the flap. Such a plan would permit some forced abduction of the fingers but would definitely lessen the blood supply passing to the strips over the individual fingers.

*Fixed adduction of the thumb* The disability which results from fixed adduction of the

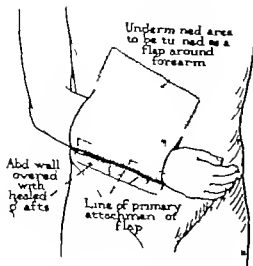


Fig. 9. Plan of procedure for surrounding entire forearm with flap of skin and subcutaneous tissue. The principle of delayed transfer is utilized both with the primary flap already attached and the part to be last applied.

tissue as a permanent covering for the hand. Its disadvantages are many. Considerable time is required during the operation to fashion the flap into a tube. If a tube is formed one must determine the amount of subcutaneous tissue raised with the skin by the tension it produces on the skin edges while the tube is being closed rather than by the desired thickness. If the tube is closed with only a little excess of tension the sutures may cut through the skin and wide separation of the edges take place. Such a complication may cause long delay in healing and completely jeopardize the success of the procedure. Finally when the tube is reopened the scar along the line of closure must be excised with some sacrifice of tissue and one may find it exceedingly difficult to leave a uniform layer of subcutaneous tissue over the entire surface of the flap. Because of these disadvantages we prefer to use a flap which is prepared in two stages, but left spread out over its original site during the period allowed for the compensatory increase of the blood supply brought to the flap through its pedicle.

#### SUMMARY OF CASES

Many men question the value of all statistical reports and the cynical reader may

TABLE I.—CAUSE OF DEFECT AND TYPE OF OPERATION CARRIED OUT

	Flap and pedicle flaps	Radial flaps	Electrical burns	Crushed injury	Injury followed by infection	Injury followed by infection	Delayed transfer	Delayed transfer	Delayed transfer	Delayed transfer
Caustic of intermediate thickness	10			20						
Whole thickness graft	22	2	4		10		20			21
Pedunculated flap	40			20	20					
Total	147	20	24	20	20	20	20	20	20	21

sometimes wonder that men with ample opportunity and abundant material do not achieve still more satisfactory results. The following statistics are reported to indicate the relative indications and usefulness of different types of grafts and flaps and the change in methods that has taken place with increasing experience. If the cases shown in Table I were grouped by years the tabulation would show that for a number of years no pedunculated flaps have been used to cover the palm and fingers except in cases of firm adduction of thumb to hand and that the only flaps which have been raised and transferred to the hand at the primary operation have been pocket flaps, almost always from the anterior surface of the thigh. With increasing experience the indications for the use of grafts of whole thickness and of intermediate thickness have been constantly widened particularly in cases of burns and injuries involving the palm. As a result time has been saved for the patient and better results have been secured both from the standpoint of function and appearance.

During a period of 20 years, the first 10 in association with Dr. Allen B. Kanavel and the past 15 in association with Dr. Michael Mason there have been under our care 431 patients with injuries of the hand and forearm which required some form of graft or flap for replacement of destroyed covering tissues. In 147 cases the defect resulted from flame or mangle burns in 90 cases from crushing injuries, in 70 cases from extensive injury followed by infection. Other causes included x ray and radium burns, electrical

burns, congenital deformities, tumors, and involvement of the skin in contractures of the palmar fascia (Table I)

In 77 cases grafts of intermediate thickness were used, in 227 whole thickness grafts, in 127 some form of pedunculated flap. Of the third group in 57 cases a flap was laid over the raw surface at the primary operation, in 70 a delayed flap was used. Of the third group a pocket flap was used in 15 cases, in 9 without preliminary elevation of the flap. In 22 patients, 4 in group 1, 11 in group 2, 7 in group 3, bilateral involvement was present which required similar treatment in both hands. In many cases several types of graft were required at different stages, for example, whole thickness grafts to separate fingers fused in an acquired syndactylism after a flap of skin and subcutaneous tissue had been applied to cover an extensive dorsal defect, and in 5 cases all three types of graft were used at some stage of the treatment. Some of the results obtained, neither the poorest nor the most satisfactory, are illustrated in the preceding pages.

#### SUMMARY

The various types of graft and flap that we have found most satisfactory in covering defects of the hand and forearm have been described, and the principles involved in their use and application detailed as exactly as possible.

The graft of intermediate thickness, of whole thickness skin and the delayed flap

raised from anterior surface of abdomen and thigh meet nearly all the indications encountered, and in our hands have proved useful in providing a resistant and permanent covering which in the majority of cases has proved satisfactory from the standpoint of appearance and function.

#### REFERENCES TO CURRENT LITERATURE

- 1 BLAIR, V. P. The full thickness skin graft. *Ann Surg*, 1924, 80, 298-324.
- 2 BLAIR, V. P., and BROWN, J. B. The use and uses of large split skin grafts of intermediate thickness. *Surg, Gynec & Obst*, 1929, 49, 82-97.
- 3 BROWN, J. B. The repair of surface defects of the hand. *Ann Surg*, 1938, 107, 952-971.
- 4 CONWAY, H. Whole thickness skin grafts in correction of contractures due to burn scars, 3 cases. *Ann Surg*, 1939, 109, 286-290.
- 5 DAVIS, J. S. The use of small deep skin grafts. *J Am M Ass*, 1914, 63, 985-989.
- 6 Idem. The use of free grafts of whole thickness skin for the relief of contractures. *Surg, Gynec & Obst*, 1917, 25, 1.
- 7 DRAGSTEDT, L. R., and WILSON, H. Modified sieve graft, full thickness graft for covering large defects. *Surg, Gynec & Obst*, 1937, 65, 104-106.
- 8 DUFOURMENTEL, L. Free full thickness skin grafts. *Bull et mém Soc d chir de Par*, 1937, 29, 306-317.
- 9 GARLOCK, J. H. The full thickness skin graft, its field of applicability and technical considerations. *Ann Surg*, 1933, 97, 259-273.
- 10 KANAVEL, ALLEN B. Congenital malformations of the hands. *Arch Surg*, 1932, 25, 1-53, 282-320.
- 11 MACCOLLUM, D. W. The early and late treatment of burns in children. *Am J Surg*, 1938, 39, 275-311.
- 12 PADGETT, EARL C. Calibrated intermediate skin grafts. *Surg, Gynec. & Obst*, 1939, 69, 779-793.
- 13 PIERCE, GEORGE WARREN and O'CONNOR, GERALD BROWN. *Surg, Gynec & Obst*, 1937, 65, 523.
- 14 REED, JEWETT V., and HARCOURT, A. K. Immediate full thickness grafts to finger tips. *Surg, Gynec & Obst*, 1939, 68, 925.
- 15 TIERNY, A. Free full thickness skin grafts. *Gaz méd de France*, 1937, 49, 795-797.

## THE PROBLEM OF HYPOPROTEINEMIA IN SURGICAL PATIENTS

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New York, New York

**C**LINICALLY hypoproteinemia is observed in a variety of conditions. Among those of special interest to the surgeon are chronic gastro-intestinal diseases, such as peptic ulcer ulcerative colitis, or regional enteritis pancreatic, biliary or intestinal fistulas chronic suppurative diseases including lung abscesses and pyarthrosis acute appendicitis and malnutrition and cachexia resulting from carcinoma. One is usually able in these cases, to attribute the deficiency in serum proteins to one of several mechanisms (1) diminished intake of food due to anorexia, vomiting or dietary restrictions (2) deficient absorption of nutritive elements from ingested food because of alterations in the mucosa of the intestinal tract or a deficiency in accessory food factors (3) severe diarrhea (4) loss of large amounts of body fluid (plasma) in extensive burns or profuse drainage from an abscess (5) decrease in the amount of absorptive area of the intestine because of operative procedures (resection or short-circuiting).

In the experimental laboratory hypoproteinemia can be induced easily by one of two methods (1) plasmapheresis or (2) restriction of dietary proteins. Furthermore, the deficiency of plasma protein thus induced can be remedied by supplying excess protein either orally or parenterally (20 30, 31 32 34, 16 19). On the basis of this work and many clinical observations, the "loss and lack" theory of the pathogenesis of hypoproteinemia was formulated. This theory postulates that hypoproteinemia is due either to a deficiency in protein intake, or to an excessive loss of protein through one of the routes mentioned above or through the urine. If this is correct, the problem of hypoproteinemia, particularly in relation to therapy is greatly simplified.

However certain facts have been determined which cast considerable doubt on the adequacy of the "loss and lack" theory.

Two problems are presented in the consideration of the pathogenesis of hypoproteinemia. First, does the "loss and lack" theory explain all the manifestations of hypoproteinemia or is there evidence pointing to the presence of a specific mechanism concerned in the production of plasma proteins, and second, is there an equilibrium between the plasma proteins and tissue proteins so that one may replace the other in times of stress.

In relation to the first, Bloomfield in 1934 on the basis of experimental work in rats, suggested that the "loss and lack" theory was inadequate to explain all the variations in serum protein deficiency and regeneration and suggested that a specific mechanism might be responsible for these variations. He makes the following statement:

"The question may be raised, however whether such a single concept (loss and lack) fits all the facts of clinical and experimental experience and whether one must not postulate in addition some injury to defect of or inadequacy of the blood protein forming mechanism as an accessory if not a primary difficulty in point of fact, the evidence for the loss and lack theory when inspected from this angle reveals a number of serious breaches.

This view is upheld by such outstanding workers in this field, as Melnick and Cowgill (20) Weech and his co-workers (30, 31 32 34) and Bing. The evidence in support of this theory is summarized briefly in the following paragraphs.

1. There is experimental evidence that loss of tissue protein and plasma proteins do not parallel one another and the maintenance of the serum protein concentration bears no relation to the nitrogen metabolism of the organism as a whole. Also dogs may utilize dietary

From the Surgical Service of Dr. Milton Bodenheimer, Hospital for Joint Diseases, New York.

protein to satisfy the nitrogen requirements of the body without adequate serum protein regeneration

2 Animals exhibit an amazing ability to regenerate serum proteins even when subject to repeated plasmapheresis. Patients likewise form serum protein easily. Therefore, protein loss, in order effectively to lower the concentration of plasma proteins, must be accompanied by a defect or impairment in the blood-protein forming mechanism, or else the plasma protein would be rapidly restored.

3 With marked loss of protein, the serum proteins do not continue to fall but maintain themselves at a constant low level. While some experimenters believe that this is accomplished by drawing on reserve protein stores, there is ample evidence that this leveling process will occur after these stores have been exhausted. This, in turn, points to the presence of a controlling mechanism.

4 There is no relationship between the initial nutritional state of dogs and the development of hypoproteinemia after plasmapheresis.

5 In Bright's disease there is no constant relation between the loss of protein in the urine and the reduction in the serum proteins. After prolonged proteinuria the serum proteins become established at a constant low level.

6 Certain infections can depress the ability of the body to regenerate serum proteins, even if ample or excessive protein is made available. This has been shown experimentally as a result of turpentine abscesses and has been observed clinically by Bruchman, D'Esopo, and Peters. We have observed this phenomenon in acute appendicitis several times. Patients who are apparently in normal nutritional status may develop a deficiency of the serum proteins very quickly following fulminating appendiceal infections.

7 In Bright's disease, a high protein diet has no appreciable effect on the concentration of the serum proteins regardless of whether there is a positive or negative nitrogen balance (1, 22).

8 There is some evidence that malnutrition may cause hypoproteinemia because of damage to the regenerative mechanism rather than as a result of a restricted protein intake.

9 In severe liver disease, the ability to regenerate serum proteins may be lost although an excess of proteins is being administered. We recently treated a case of acute yellow atrophy of the liver in which the serum proteins fell to a seriously low level and remained there in spite of a diet very rich in protein and daily blood transfusions.

On the basis of the clinical and experimental evidence adduced in the preceding paragraphs one must conclude that there is undoubtedly a specific mechanism which controls the formation of serum proteins. This is of great importance in therapy, for if this mechanism is impaired it is obviously futile to administer large amounts of proteins which cannot be utilized to regenerate serum proteins. This may explain the failure, clinically, to restore proteins to normal even though all routes of administration are employed, and the amounts ingested are sufficient. In connection with this the second question raised assumes importance. If there is a reciprocal equilibrium between tissue and plasma proteins then one can draw from the other in times of stress. Holman, Maloney, and Whipple state that there is a "dynamic equilibrium between tissue proteins and plasma proteins which is governed by the physiological needs of the moment." While this is true to a certain extent, it does not mean that tissue proteins or the products of tissue protein catabolism can be utilized to form new serum proteins. However, the reverse of this reaction, namely, the conversion of plasma proteins into tissue proteins can and does occur. Undoubtedly there are certain reserves from which serum proteins can be regenerated, but once these are exhausted, no further aid may be expected from the tissue proteins. Whipple describes three types of tissue proteins: (1) the labile reserve protein which is readily available for serum protein regeneration, (2) the dispensable reserve protein which is less readily available, and (3) the indispensable and fixed protein of the body cells which is never available. This division makes available a certain amount of reserve protein, but when this is exhausted, the serum proteins can no longer draw on the tissues for replenishment. Thus, although the plasma protein does contribute to the protein needs



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concentration of the serum protein which is first found in association with clinical edema. They state

"The critical level of protein in the serum is determined by that concentration which permits the attainment in the tissue spaces of mechanical pressures great enough to break down the restraining action of the connective tissue boundaries of the spaces. Obviously such pressures can occur only when the colloid osmotic pressure of the serum has fallen below the capillary blood pressure, but the effect of the fall on pressure outside the capillaries is more directly the cause of edema than the disturbance of the balance between the internal forces."

This factor of tissue elasticity is of importance for the reason that with increasing stress on the tissues as a result of declining serum proteins, there is expansion of the intracellular space for some time prior to the appearance of edema. When the stress becomes too great, that is, when it overcomes the elastic strength of the tissue framework, the tissues seem to be torn apart and palpable edema results.

We may then state that edema is a result of a disturbance in the balance between two forces. On one side there is the colloid osmotic pressure of the blood less that of the tissue fluid, and on the other, the effect of the hydraulic pressure of the capillary blood pressure, less the pressure due to the elasticity of the tissue spaces. This concept enables us to explain many vagaries in the appearance of edema. It is well known that no actual critical level for edema is universally present. Edema may occur in some cases at a concentration of 6 grams per cent of serum protein and be absent in other cases at a level for the proteins of 5 grams per cent. It is also well known that there are certain sites of predilection for the appearance of edema, and these are in the soft, elastic, subcutaneous space. Finally, the effect of physical activity on the pressure in the tissue spaces may influence the appearance of edema. These phenomena can best be explained by the theory outlined above.

The principal constituents of the serum proteins are the albumin and globulin fractions.

The normal range for the serum albumin is from 3.5 to 5.0 grams per cent, while for the globulin fraction the range is from 1.5 to 2.6 grams per cent. The albumin and globulin have no chemical similarity and bear no quantitative relationship to each other. There is actually no significance to the albumin-globulin ratio inasmuch as each is affected by different conditions and the concentration of one constituent in the plasma has no effect on the concentration of the other. Serum-globulin may be increased in the chronic infections, syphilis, lymphogranuloma venereum, and tuberculosis. Albumin is diminished in cases of malnutrition and extensive loss of serum protein. In patients with hypoproteinemia the globulin concentration is not commonly decreased, while the albumin fraction is very low. Govaerts (8, 9) estimated the osmotic pressure of serum albumin and globulin independently. He determined that the osmotic pressure of albumin is 5.5 millimeters of mercury for every 1 gram per 100 cubic centimeters while that of globulin is only 1.4 millimeters of mercury for every gram per 100 cubic centimeters. Accordingly the total oncotic pressure of normal serum varies from 21 to 29 millimeters of mercury per 100 cubic centimeters. This explains the importance of lowered albumin concentration in the production of edema, and the relative insignificance of variations in the globulin content. While a decrease of 2 grams per cent of albumin would lower the oncotic pressure of the blood approximately 11 millimeters of mercury, a similar change in globulin would mean a decrease of only 2.8 millimeters of mercury. Palpable edema will almost invariably be present when the albumin fraction falls below 2.5 grams per 100 cubic centimeters and is rarely found when concentration of this fraction is over 3 grams per 100 cubic centimeters. With these values for albumin, the globulin may be normal, increased, or decreased but the effect on edema will be insignificant. Various authors (21, 13, 33), state that edema will occur at levels for the total serum proteins of  $5.5 \pm 0.3$  grams per 100 cubic centimeters but as has been shown, the figures which are presented are susceptible to definite fluctuations.

of the body cells and an animal can be kept in nitrogen equilibrium and weight equilibrium by the administration of proteins intravenously and carbohydrates and fat by mouth the body proteins contribute only with difficulty to the plasma protein. This has been summarized by Pommerente Slavin, Karchen and Whipple as follows: In an emergency the plasma proteins may contribute to body proteins but the current will not flow easily in the opposite direction and the body proteins may be said to stand by helpless to aid while vital plasma proteins are depleted even to a lethal point. Evidently in this emergency the plasma protein is very largely if not wholly dependent on materials coming in from the gastro-intestinal tract.

Recent evidence has tended to implicate the liver as an important if not the specific mechanism concerned with serum protein regeneration. Whether this is confined to the liver or to the entire reticulo-endothelial system is still a moot point. Whipple points out that the liver participates in the "assembly of amino-acids and other constituents of body proteins into aggregates which may be used in the liver or elsewhere to form specific proteins of the body cells. Weech suggests that liver disease interferes with regeneration of serum proteins and believes that the liver may be affected in prolonged malnutrition so that return to normal of the serum proteins is markedly delayed even when adequate feedings are resumed. Johansen reports hypoproteinemia in cases of liver disease and expresses the opinion that the liver assumes a rôle of major importance in the synthesis of proteins. Many workers have called attention to the damage sustained by the liver as a result of surgery and anesthesia, particularly in cases of the hepatorenal syndrome. It is possible that lesser degrees of damage may be responsible for the hypoproteinemia which is occasionally encountered in surgical cases and which is so resistant to treatment by replacement therapy

extracellular fluid. Starling in 1898 first postulated that the movement of fluid between the vascular channels and the interstitial spaces is governed by two factors (1) the capillary blood pressure and (2) the colloidal osmotic pressure of the blood. The former tends to force fluids into the tissues while the latter draws fluid from the interstitial spaces into the blood stream. He emphasized the rôle of the plasma proteins in this interchange. The colloid osmotic tension which is largely determined by the concentration of plasma proteins counterbalances the mechanical effect of the hydraulic pressure in the capillaries (the capillary blood pressure). The proteins, to which the vascular walls are normally impermeable produce an osmotic pressure difference between the serum and the relatively protein free interstitial fluid with which they are in diffusion equilibrium and this is sufficient to counterbalance the effect of the capillary blood pressure. In health this oncotic pressure is greater than the mean capillary pressure and will absorb any excess of fluid in the tissue spaces (14, 15). Krogh postulates that there is thus a "margin of safety" which keeps the fluid in the vascular channels and the interstitial fluid in equilibrium and prevents edema.

According to this theory edema will develop when the oncotic pressure is low in relation to the capillary blood pressure and this may occur as a result of one of the following: (1) loss of serum proteins, (2) increase in capillary pressure as in venous obstruction, or (3) the vessel walls become pervious to proteins as in inflammatory states or vasomotor paralysis (22). Recent work, however has demonstrated that the mechanical forces of the interstitial tissues must be considered in the production of edema. These forces consist of two factors: (1) the oncotic pressure of the tissue fluids based on the protein content, which, however is very low in filtration edema fluid and therefore is of little significance, and (2) the tissue tension or elasticity (26). Weech and his co-workers (30, 31, 32, 34) suggest, as a result of their studies that there is no definite critical level of the serum protein for the production of edema, but rather a correlation level which pertains to that

#### RELATIONSHIP BETWEEN PLASMA PROTEINS AND EDEMA

It has been established by experimental and clinical evidence that the plasma proteins are the dominating factor in the distribution of

(1) the production of peripheral edema, (2) the production of visceral edema, and particularly pulmonary edema, (3) the inhibition of gastro-intestinal activity, and (4) the inhibition of wound healing. Frequently all of these are noted in the same patient.

**Peripheral edema** This is usually the earliest and most frequent manifestation of hypoproteinemia. There are certain sites of predilection for this edema, notably in the loose areolar tissue of the subcutaneous spaces. The abdominal wall, the back of the ankle, the legs, and the face are the common sites. It is this symptom which, as a rule, calls the attention of the surgeon to the deficiency which exists in the concentration of the serum proteins, and while not in itself a serious complication, it forewarns of others far more serious. It indicates a severe nutritional disturbance which may not be confined to the blood, and which requires intensive treatment. As pointed out previously, the normal human regenerates serum protein with amazing rapidity so that when a deficiency exists and is manifested by the early signs of fluid unbalance, one must consider not only whether nutrition is disturbed but whether the mechanism for regenerating protein has been impaired. Occasionally the occurrence of peripheral edema causes no change in the general attitude or reaction of the patient. We have observed, however, that most patients react unfavorably to this development. They are frequently irritable and restless, and may have anorexia, nausea, and vomiting. Rarely they may become irrational. A typical case report is presented.

**CASE 1** E Z, hospital No 69224. A 6 year old white child was admitted to the service of Dr M Bodenheimer on February 28, 1938. She had been severely burned by a gas stove. Examination revealed extensive second degree burns of the right arm, forearm, hand, and the posterior aspects of the right arm and leg, both buttocks, and the back. After a preliminary cleansing of the burned areas, she was treated by the tannic acid silver nitrate method. Fluids were administered parenterally. On admission, marked evidence of hemoconcentration was present. Examination of the blood revealed 16 grams per cent of hemoglobin and a red blood cell count of 6,400,000 per cubic millimeter. In about 1 week, after fluid balance had been restored, the hemoglobin estimation showed 11.8 grams per cent and the red blood count was 4,960,000 cells. The patient reacted well to the local therapy, but on March 3, 3 days after admission, her serum proteins totalled only 5.3 grams per 100 cubic centimeters. The albumin fraction was 3.5 grams per cent and the globulin 1.8 grams per cent. The following day, peripheral edema appeared involving the back, neck, face, and extremities. The child was placed on a high protein diet and given glycolixir tablets by mouth. In addition repeated transfusions were administered. Table I summarizes the further course.

It is evident from this case that several factors were involved in the protein depletion. Initially, loss of fluid and plasma from the burned areas caused marked hemoconcentration and initial depletion of the plasma proteins. The hemoconcentration was controlled by the administration of sufficient fluid and electrolytes as evidenced by the drop in hemoglobin from 16 grams to 11.8 grams per 100 cubic centimeters in 2 days. During this time, in spite of high protein diet and several transfusions, the serum protein remained low. When the initial infection was controlled the serum proteins returned to almost normal figures. Then when the serious secondary infection occurred, the serum protein concentration again fell and edema recurred. Intensive administration of protein during this period had no effect on the falling proteins of the serum, indicating that regeneration was not taking place. During this

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Date	Serum proteins gm. %			Hb gm %	R.B.C. million	Course
	Alb	Glob	Tot			
3-7	2.7	1.3	4	11.8	4.96	Edema still present. Anorexia irritability
3-14	2.7	2.6	5.3	11	4.00	Edema subsiding. Infection under eschar
4-10	3.6	2.5	6.1	10.4	3.84	Infection under control. No edema. General condition much improved. Thiersch grafts on 4-30-38
6-1	2.8	2.8	5.6	7	2.81	Infection recurred. Granulations very sluggish. Child is very toxic. Transfusions given repeatedly
6-6	2.8	2.8	5.6			Slight peripheral edema. Unchanged
6-27	4.4	3.2	7.6	12	4.22	Much improved. No infection
7-8	4.5	2.9	8.4	10.5	3.74	Much improved. Additional Thiersch grafts on 7-2 taking well

#### RELATIONSHIP BETWEEN PLASMA PROTEINS AND OTHER FACTORS RESPONSIBLE FOR EDEMA

It is well known that the distribution of body fluids is affected by many factors. While the serum proteins are among the most important, the rôle of the electrolytes should not be underestimated. Variations in the character concentration, and distribution of the acid and base electrolytes will cause marked changes in the hydration of the human body. In the healthy subject, an excess of sodium chloride ingested through the gastro-intestinal tract will be promptly excreted by the kidneys. If a sufficiently large excess of salt is ingested and the fluid intake controlled, dehydration of varying severity will be induced by the excretion of the excess salt in solution thus the body fluids will be depleted. If however the kidney is diseased or its function impaired as it is so frequently in the seriously ill surgical patients, salt given in excess will be retained in the body and will cause the retention of water in an effort to maintain the proper electrolyte concentration of the body fluids. As a result of this mechanism by which the electrolyte concentration is protected from excessive fluctuation edema is produced. This edema will also be adversely affected by hypoproteinemia if this should be present. On the other hand hypoproteinemia existing in conjunction with dehydration may not cause edema, regardless of the degree of the deficiency because retention of fluid in these cases would seriously interfere with the concentration of electrolytes.

In patients who because of vomiting, diarrhea, or other causes, have had an excessive loss of electrolytes, this same protective mechanism will result in loss of body fluids until the correct concentration of electrolytes in the body fluids is established. Hemoconcentration and dehydration are the sequelae of this chain of events. Hemoconcentration, as determined by studies of the hematocrit and specific gravity values will alter the values for all blood constituents. A patient who is dehydrated may show a serum protein value of 7.0 grams per 100 cubic centimeters or over. However when sufficient fluid and salt are administered to overcome the dehydration the true value for the proteins can be deter-

mined and this may be definitely below edema levels. Edema will then result and if one has not carefully considered the changing relationships of plasma proteins, blood concentration, and electrolytes, this edema may be attributed erroneously to excessive salt administration. It is of the utmost importance therefore, in administering fluid to sick surgical patients to evaluate carefully the aforementioned factors. The amount of fluid to be administered can be determined by studies of the specific gravity of the blood and the hematocrit, while the character of the fluid to be given (i.e. saline, distilled water, whole blood, or plasma) can be determined by studies of the plasma chlorides and plasma proteins.

#### CLINICAL MANIFESTATIONS OF HYPOPROTEINEMIA

The clinical manifestations of hypoproteinemia are chiefly dependent on the alterations in the fluid distribution of the body which are induced by this state. Various organs may be affected, giving rise to what may appear to be dissociated symptom complexes. These symptoms and signs, however are simply the external and palpable evidence of a profound physiological and nutritional disturbance. Reduction of the total serum protein below 3 grams per 100 cubic centimeters is usually considered to be incompatible with life. In the range between this figure and the normal, various disturbances are observed. Often, the severity of the clinical picture does not parallel the reduction in serum proteins and marked disturbances are noted with but slight variations in the proteins. In addition various other factors may influence the clinical picture. Disturbances in the nutritional state as a result of avitaminosis or dehydration profoundly affect the signs and symptoms caused by hypoproteinemia. For example a deficiency of vitamin B complex may augment the inhibitory effects of diminished serum proteins on the intestinal tract, while lack of salt or dehydration may delay the appearance of edema. In a consideration of nutritional disturbances all factors must be thoroughly evaluated.

The effects of hypoproteinemia may be divided conveniently into four categories

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latter interval a severe secondary anemia and infection were present. It is conceivable that because of the anemia and infection sufficient damage to the blood forming mechanism took place (in the liver?) to render it unable to utilize the proteins administered through the gastro-intestinal tract. During this period of hypoproteinemia the granulating areas were edematous and epithelialization was almost absent. Finally when the infection responded to treatment both the hemoglobin and the proteins returned to normal.

The striking point in the progress of this patient was the parallelism between the general condition and the presence or absence of edema. When edema was present the child was irritable apprehensive and feeding had to be forced. With an improvement in her serum proteins (and incidentally in her hemoglobin values) the entire picture changed and she became more alert and seemed generally improved. We have noted this in other cases, and while we have not been able to elicit definite neurological signs of any significance in these cases, we have speculated on the possibility of the presence of some cerebral edema.

*Visceral edema.* In this category we are primarily interested in pulmonary edema. Jones and Eaton have pointed out that the edema resulting from hypoproteinemia frequently involves the parenchymatous organs, and they reported 5 cases of pulmonary edema, one of which ended fatally as a result of hypoproteinemia. Apparently the lung is one of the sites of predilection for edema in these cases.

We have observed this complication several times and believe that it occurs much more frequently than it is recognized. Pulmonary complications occurring in the postoperative course are usually diagnosed as atelectasis or pneumonia but frequently neither the course nor the roentgenographic examination confirms this diagnosis.

Transient pulmonary edema of a mild grade may simulate a pneumonic process and may be incorrectly diagnosed if the true nature of the causative factor is not recognized. Occasionally the edema of the lungs may occur very quickly and be the direct cause of death even though no cardiac decompensation is present.

It is a debatable point whether pulmonary edema can be caused by the excessive administration of fluids without excess of salt in the postoperative period. Undoubtedly when cardiac decompensation is present pulmonary edema may occur as a result of right-heart failure. In the absence of cardiac weakness it is unlikely that pulmonary edema will result from over-administration of fluids unless sodium chloride in great excess is likewise administered or hypoproteinemia is present. As a matter of fact, administration of glucose in distilled water may have a dehydrating effect on the body. Glucose even though administered in an isotonic (5 per cent) solution does not act in the same manner as salt solution in retaining fluids in the body. The glucose is metabolized leaving distilled water which is excreted with some of the body salt in the urine and in this way causes a loss of interstitial water to maintain the electrolyte concentration at normal (?). In those cases in which fluid has been pushed to the point of water intoxication cerebral edema will occur and cause death but pulmonary edema is not marked. While indiscriminate administration of fluid is to be condemned strongly it often becomes necessary to administer from 4000 to 5000 cubic centimeters in one 24 hour period to restore the salt and water balance of a patient. Occasionally a surgeon may hesitate to administer this amount because of the erroneous assumption that it will cause pulmonary edema. This fear as has been pointed out above is entirely without foundation if the cardiac status is good. The real dangers of dehydration are far more important than the feared ones of water-logging but if fluid is administered according to a rational method, neither of these should occur.

In patients with hypoproteinemia, on the other hand pulmonary edema can occur with the administration of minimal amounts of fluid and even though the patient is in negative water balance. In contrast to the parenchymatous edema resulting from water intoxication, the edema resulting from hypoproteinemia frequently involves the lungs. In the following case the pulmonary edema was considered largely contributory to the lethal outcome.

CASE 2 F E, Hospital No 80006, was admitted on November 11, 1939, with signs and symptoms of acute appendicitis. Laparotomy was performed immediately and a perforated gangrenous appendix was removed. There was a moderate amount of free, purulent fluid in the peritoneal cavity. The wound was drained and closed in layers. The patient developed a severe grade of paralytic ileus which was treated with a Miller-Abbott tube. On the fifth day after operation mild peripheral edema was observed, and on the following day the serum protein concentration was 5.4 grams per 100 cubic centimeters. Two days later complete dehiscence of the abdominal wound occurred without obvious signs of infection. This almost characteristic manifestation of the hypoproteinemc state will be considered in connection with another case. Several transfusions were given but the edema persisted and the patient became progressively more toxic. The salt and fluid balance was carefully watched and because of the edema, the patient was kept slightly below a positive balance. In spite of these precautions the serum proteins showed no improvement and on November 24, 1939 the concentration was still 5.4 grams per cent. On the fourteenth day after operation sudden pulmonary edema developed which did not respond to oxygen therapy or transfusions. There were no signs of heart failure. The edema progressed and peripheral edema became more marked until death of the patient ensued 2 days later.

*Disturbances of gastro-intestinal motility*  
Hypoproteinemia exerts a definite inhibitory effect on the motility of the gastro-intestinal tract. This has been observed in dogs by Mecray and his associates who found that an increase in the gastric emptying time accompanied hypoproteinemia. This occurred in dogs with intact stomachs and in those upon whom short-circuiting operations had been performed. Clinically, this phenomenon has been observed repeatedly. Jones and Eaton reported a case of fatal intestinal obstruction in a patient with hypoproteinemia and others have detected obstructions of varying degrees. We observed a patient who, immediately after a subtotal gastrectomy for ulcer, developed all the signs of an upper intestinal obstruction. Laparotomy revealed thickened and edematous loops of bowel with edema at the gastro-enterostomy stoma. No other obstructive mechanism was found. Unfortunately no studies of the serum proteins were made but in view of our experience in subsequent cases we feel that this was definitely a result of hypoproteinemia.

Frequently, it is found that persistent vomiting will occur after gastro-enterostomy or operation on the bowel. Inasmuch as these patients are in a poor nutritional state, hypoproteinemia develops quickly following operative procedures, and particularly after those which necessitate abstinence from oral feeding. This leads to edema of the stoma and the intestinal wall and a picture resembling acute obstruction develops. Roentgenographic examination is of little value as it merely confirms the presence of obstruction without demonstrating the etiological factor. Whether the obstruction or diminished motility is due entirely to the edema of the stoma with consequent narrowing or to edema of the entire thickness and extent of the gastric and intestinal wall which interferes with effective muscular contraction is debatable. Mecray, Borden, and Ravdin believe the former to be true on the basis of fluoroscopic examination of dogs following a barium meal. They found that, while motility was almost absent in hypoproteinemc dogs, intestinal peristalsis and tone were normal.

When the serum proteins are restored to normal the obstructive symptoms quickly subside and the clinical improvement of the patient is marked. This is further evidence of the importance of the proteins in causing this complication. Inasmuch as these patients are poorly nourished they frequently present vitamin deficiencies which augment the effect of the hypoproteinemia on gastric motility. This is particularly true of vitamin B, which therefore, should be administered in conjunction with proteins. Recently Stengel and Ravdin have suggested the use of the Miller-Abbott tube for feeding purposes following gastric or intestinal operations. The end of the tube is pulled through the stoma and feeding of proteins is started immediately following the operation. This is well tolerated and is effective in aiding the restoration of proteins in the serum.

Case report M M M, No 72350, a white male, 54 years of age, was operated upon for a carcinoma of the stomach and a Pólya type of gastrojejunostomy performed on September 9, 1938. His pre-operative status was good and he was considered a good operative risk inasmuch as his symptoms had been present for only 4 months and he had been



eating well. His blood chemistry before operation was normal the hemoglobin was 3 grams per 100 cubic centimeters, the red blood cells numbered 4,640,000 per cubic millimeter. Following the operation vomiting commenced and was persistent. Wangersteen suction was instituted on the second day after operation and was continued for 3 days. Vomiting persisted and on the thirteenth day peripheral edema of the extremities was noted. At this time the patient was dehydrated and the total proteins of the serum were 6.1 grams per 100 cubic centimeters. We felt that this value was misleading because of hemoconcentration and instituted a high protein diet. Roentgenogram revealed no small intestinal obstruction. The high protein diet of easily assimilable materials was continued through an indwelling tube but on the eighteenth day after operation the serum proteins were reduced to 5.1 grams per 100 cubic centimeters which we took to be a truer index because hydration had been accomplished by this time. Proteins were pushed and 3 days later vomiting had completely ceased. When the vomiting stopped the serum proteins had been increased to 5.7 grams per 100 cubic centimeters which although low was apparently above the edema level. The remainder of the course was uneventful.

This case illustrates two very important factors. In the first place estimation of total serum proteins must be done in conjunction with studies of blood concentration. We now routinely do hematocrit studies in order to judge hemoconcentration more accurately. The McAure Aldrich test for dehydration has not been sufficiently accurate in a very small series of cases in our hands but we are studying this method further. Second it illustrates that hypoproteinemia can develop rapidly following serious operations even though the patient is in apparently good nutritional balance before operation.

*Disturbances in wound healing.* Experimental work on wounds has demonstrated that the principal essential for rapid healing is multiplication and growth of fibroblasts. Harvey and Howe have divided the period of wound healing into three phases (1) the lag period (2) the period of fibroplasia when the velocity of healing is changing most rapidly and (3) the phase of approaching maximum immediate strength. Clarke in 1919 in studying the effect of diet on the healing of wounds determined that a high protein diet shortened the lag phase and produced a decrease in the time necessary for initiation of the growth of

fibroblasts. He believed that proteins were necessary for proper wound healing. Harvey and his co-workers have also emphasized the importance of proteins but they believe that the lag phase is not affected. They have found an increase in the velocity of growth of fibroblasts with a high protein diet but no change in the duration of the lag phase or in the maximum strength of the healing wound, although this last phase is reached sooner. Thompson and his associates first demonstrated that an artificially induced hypoproteinemic state in dogs interfered with the healing of visceral and surface wounds in over 70 per cent of the animals. In these cases either disruption of the wound or delayed healing occurred, but when the serum proteins were restored to normal by the administration of lyophilized plasma, wound healing rapidly occurred (29).

This interference with wound healing associated with hypoproteinemia has been observed frequently by us. In 1 case previously reported (4) complete disruption of the abdominal incision occurred and secondary suture failed to cause healing. The serum proteins of this patient were consistently below 3.5 grams per 100 cubic centimeters and all efforts to raise the level were fruitless. Needless to say death quickly ensued. In Case 2 disruption of the wound also occurred and though an appendiceal abscess was present, the wound was not grossly infected, and presented the edematous appearance common to these patients. In the cases observed by us, the wounds were clean, edematous, glistening, pale, and anemic in appearance. These findings have been reported in hypoproteinemic dogs by Thompson. The question of whether edema *per se* will cause delay or absence of wound healing is to be seriously considered. While the evidence of the importance of proteins in accelerating fibroblastic proliferation is conclusive, it is well known that incisions into edematous tissues usually heal poorly. Thompson, in the studies referred to found that edema of the wound edges persisted for varying periods after the serum proteins had been restored to normal and this did not inhibit repair of the wounds. It is probable that both factors i.e. specific absence of protein

(or possibly of certain amino acids) and the resulting tissue edema, operate to delay wound healing in these cases. It would be interesting to produce edema by excess salt administration and maintain the serum proteins at a normal level and study the effect on experimental wounds.

**Case report.** A R., No 78483, a white male, 16 years of age, was operated upon for an appendiceal abscess on August 19, 1939. On the tenth day after operation signs of a mechanical intestinal obstruction developed and on August 31, 1939, the abdomen was opened through a suprapubic incision. A strangulating, adhesive band obstruction was found and released. A small perforation of the ileum was closed by a pursestring suture and the wound closed without drainage. On September 9, extensive edema of the thoracic and abdominal wall and hydrothorax was noted. The serum proteins were 5.5 grams per cent and the albumin was reduced to 3 grams per cent. Marked distension occurred but was controlled with a Miller-Abbott tube. On September 13, the second incision disrupted but no evisceration occurred. The serum proteins were unchanged from the level of the previous examination. Hydrothorax, pulmonary edema, and edema of the face and hands soon followed. Multiple transfusions were given and a high protein diet administered through the indwelling tube. On September 18 the edema had largely disappeared and by October 1 it had completely disappeared. Healing of both wounds had remained practically stationary during this period. On October 2 the serum proteins had risen to 8.6 grams per cent and the albumin fraction was 4.8 grams per 100 cubic centimeters. After this healing became much more rapid and the remainder of the course was uneventful.

In this case again, the warning sign of peripheral edema antedated wound disruption but was overlooked, no transfusion or protein therapy being instituted until after dehiscence occurred. We cannot stress too strongly the importance of the early signs of hypoproteinemia which, although probably innocuous in themselves, should direct our attention to the underlying nutritional state before more serious sequelæ occur.

#### TREATMENT

The treatment of hypoproteinemia should be prophylactic. All patients about to undergo serious operative procedures should be carefully studied for disturbances in their nutritional status, with particular reference to serum proteins, vitamins, and fluids. If

actual depletion of serum proteins is discovered, the operation should, if possible, be postponed until the normal concentration is restored. It is much easier to do this before than after operation and frequently a high protein diet will suffice. If the patient is unable to retain or absorb the necessary food elements when administered by mouth, other methods which will be described subsequently must be instituted. Unfortunately, however, the presence of severe nutritional disturbances as manifested by hypoproteinemia is not usually discovered until complications ensuing in the postoperative period indicate that the protein metabolism is disturbed.

The restoration of diminished serum protein to normal is not always a simple task and is dependent on two factors: (1) whether there is damage to the regenerating mechanism, and (2) whether the abnormal loss of protein can be stopped. As a rule, the second factor can be controlled without much difficulty or sufficient protein can be administered to counteract this loss. The first factor, however, is much more significant. If the ability of the organism to regenerate the proteins of the serum is impaired or destroyed, no amount of protein which can be administered will do more than act as a temporary substitute for the proteins already lost. As yet, no method whereby this mechanism can be sustained or repaired is known, and, as a matter of fact, the nature of the mechanism is still in doubt. There is some evidence that the liver or possibly the cells of the entire reticulo-endothelial system are the site of the formation of serum proteins and as is well known, these cells are frequently injured or their function impaired. Among other factors, anesthesia, sepsis, and anoxemia may adversely affect these structures and interfere with their protein regenerating function. It is in these patients that the problem of sustaining the level of serum proteins assumes such magnitude. We have seen such cases, and have seen many case reports in the literature, wherein the serum proteins were diminished and could not be replenished despite the administration of large amounts of protein. Recently a patient was observed who was suffering from acute yellow atrophy of the liver and in whom a severe hypoprotein-

emia developed. It was impossible to raise his protein concentration appreciably despite the administration of large amounts of protein by mouth and repeated massive serum transfusions. In this case the mechanism for regenerating serum proteins was seriously inhibited. Other patients exhibit this same phenomena without obvious liver disease and they present the same great problem in therapy.

The administration of protein by mouth either as whole proteins or amino acids is obviously of no value as these cannot be utilized and synthesized to form serum protein. By supplying the necessary protein in a utilizable form serum transfusions are a temporary expedient but they may be sufficient to carry the patient until any injury to the serum regenerating cells may have time to heal. Occasionally this is inadequate and the patient eventually dies of this deficiency. McNick and Cowgill have stressed the point that until the nature of the mechanism which controls the regeneration of serum proteins is better understood the approach to therapy can be only symptomatic and haphazard.

It is fortunate that many if not most of the surgical patients who develop hypoproteinemia exhibit no serious defect in the regeneration of serum proteins. The deficiency is usually amenable to treatment without much difficulty and consequently we feel that the impairment in the mechanism of protein regeneration is slight. It is debatable whether administration of proteins acts as a stimulant to serum protein regeneration, and Weech (30, 31, 32, 34) was unable to determine any correlation between the administration of proteins and the rate of regeneration. There is, however, some experimental work which indicates that malnutrition may affect the liver and impair its ability to synthesize serum proteins. Probably the restoration of the nutritional state to normal remedies this disability; at any rate it is an established fact that very frequently the proper administration of protein does replenish the serum proteins and overcomes hypoproteinemia with its concomitant manifestations. In this connection the administration of large amounts of glucose may be of value because of the beneficial

effect on the liver and because of its caloric value.

Proteins may be given by mouth, by rectum or parenterally. Unquestionably the method of choice when feasible is the oral route. The absorption of the split products of protein digestion normally occurs in the small intestine and in the ordinary course of events the material for building serum proteins is obtained in this way. In the pre-operative period little difficulty is encountered in administering sufficient proteins by mouth. For some time we have been preparing our surgical patients by feeding a diet containing 25 per cent of proteins for several days or a week before operation. Occasionally patients are unable to take or retain food by mouth because of their surgical condition. The presence of peptic ulcers, pyloric obstructions, intestinal fistulas and other similar conditions may contra-indicate oral feedings. In these cases we have frequently been able to institute feedings through an indwelling tube. Recently Stengel and Ravdin have reported an excellent method of administering protein through a Miller Abbott tube by using an intermittent pressure pump. They have had considerable success with a peptone hydrolysate mixture. We have used whole protein in our patients with good results. In the post-operative period oral feedings are usually contra-indicated and at this time the device of Stengel and Ravdin is of immeasurable value. Following gastric resection or gastro-enterostomy the tube is drawn through the stoma and feeding can be started almost immediately. We have had no experience with rectal feedings of proteins but the work of Ravdin and of Rhoads and his co-workers seems to indicate that some absorption of protein split products does take place in the colon and this route may be utilized if necessary.

The parenteral administration of proteins is invariably by the intravenous route. Whole blood or plasma are the two agents most commonly employed. The use of whole blood is of particular value when hypoproteinemia is associated with anemia. It is important to give multiple, large, and frequent transfusions if a definite rise in the serum proteins is to be

obtained and maintained. We have noted elevations of 0.2 to 0.4 grams per 100 cubic centimeters immediately following transfusion of 500 to 1000 cubic centimeters of blood but within 24 hours this may be lost if further transfusions are not administered. The use of plasma or serum presents several advantages over whole blood. In the absence of anemia, it does not overload the circulation with red blood cells which are not needed. Secondly, it may be stored indefinitely without deterioration, in marked contrast to whole blood, and thirdly, if pooled serum is used, it need not be of the same type as the patient's blood. Plasma or serum transfusions afford a method of administering concentrated serum protein quickly and easily, and with a minimum of reaction. Our experiences have been very satisfactory but the admonitions in regard to the use of whole blood must be carried out. Frequent and large infusions must be given. We have administered 1000 cubic centimeters of plasma several times and have noted no untoward reactions.

The use of desiccated or lyophilized plasma described by Flosdorf and Mudd has been suggested but we have had no experience with this preparation. Ravdin, Stengel, and Prushankin report severe reactions following the use of lyophilized plasma. Recently Elman and Weiner reported their experiences with the administration of amino acids derived from the hydrolysis of casein with the addition of tryptophan and cystin. They have used this mixture in many cases without any demonstrable deleterious effects and in many cases were able to elevate the serum proteins appreciably. In many cases, however, despite apparent clinical improvement, no rise in the serum proteins was observed. In these cases, doubtlessly, the temporary clinical improvement was attributable to the transient increase in the osmotic pressure of the blood but apparently no regeneration of proteins occurred in the patient. Whereas amino acids when given intravenously must be synthesized into serum proteins within the organism, plasma is immediately available for use and hence serves as a more efficient substitute for the lost proteins. However, when there is no striking interference with the regenerative

function of the patient, it would seem that amino-acids should be of great value. At any rate this method of "intravenous alimentation" has great possibilities in the treatment of temporary diminutions in the serum protein level, and is certainly worthy of further study. The importance of the proper selection of amino-acids cannot be overestimated, however. It has been demonstrated conclusively that certain amino-acids are indispensable for serum protein regeneration. Both cystin and tyrosine must be present, either in the diet or in the parenteral medication, to provide the necessary elements for the formation of the protein of the serum (17). While phenylalanine and methionine are indispensable for tissue growth they play a minor rôle in the rebuilding of the serum protein. This has been recognized by Elman and his associates in planning the character of the intravenous solutions they employed.

It would seem from the foregoing that the therapy of hypoproteinemia rests on an insecure foundation. Fortunately, the majority of cases are either improved or cured by the substitution of serum proteins or by the administration of the essential elements which constitute these proteins. In the cases resistant to this therapy, attention must be given to the liver. There is ample evidence that a high protein intake in addition to carbohydrates is essential to protect the liver from damage by anesthetic agents or other noxious substances. This consideration should guide our pre-operative as well as postoperative care and may prevent hypoproteinemia from developing. We feel that the use of large amounts of intravenous glucose in a 10 per cent solution in distilled water plus a high protein diet by mouth or through an indwelling tube is the best means of preparing the liver for the shock of surgery, or treating it when it has already been damaged. In addition, the free use of plasma transfusions has, in our hands, been the surest and swiftest method of causing at least temporary rises in the serum proteins in hypoproteinemic patients.

#### SUMMARY AND CONCLUSIONS

1. Evidence is presented which suggests that hypoproteinemia is caused by impair-

ment of the mechanism or organ which is responsible for the production of serum proteins. The loss and lack theory does not explain the variations in the metabolism of serum proteins.

2 There is some evidence to indicate that the liver is the site of regeneration of serum proteins.

3 Edema is a result of hypoproteinemia. This edema is attributable to alterations in the mechanics of fluid distribution between the vascular channels and the extravascular spaces which are caused by a decrease in the colloidal osmotic pressure of the blood induced by a deficiency of the serum albumin. However many other factors may influence this edema. Among these are the following: tissue elasticity, water balance, and the character and distribution of the electrolytes of the body fluids.

4 The clinical manifestations of hypoproteinemia are varied but almost all can be explained on the basis of disturbances in fluid distribution. The principal manifestations are peripheral edema, pulmonary edema, disturbances in gastro-intestinal motility and disturbances in wound healing.

5 Treatment is not always satisfactory inasmuch as the exact mechanism responsible for the production of serum proteins is unknown. Since the liver plays a definite and important rôle, therapy should be directed toward protecting and sustaining this organ. A high protein and carbohydrate intake is essential.

6 Substitution therapy in the form of whole blood or plasma transfusions, parenteral administration of amino acids, or orofejunal feeding of amino acids, has met with some success. In our experience the administration of massive transfusions of plasma has provoked the greatest and most sustained rise in the serum proteins.

#### REFERENCES

1. BIDO, J. *Studies on Proteinuria Albuminuria*. Dissertation. Copenhagen. Levin and Munksgaard, Ejner Munksgaard, 1934.
2. BLOOMFIELD, A. L. The effect of restriction of protein intake on the serum protein concentration of the rat. *J. Exper. Med.* 913, 57-705.
3. B. OCKMAN, F. S. D'ANGELO, L. M. and PETER, J. P. The plasma proteins in relation to blood hydration. *J. Clin. Invest.* 930, 8-377.
4. CARTER, D. *Nutritional disturbances in repair*. *entails*. *Surgery* 930, 6-705.
5. ELKAM, R., and WINTER, D. O. Intravenous administration. *J. Am. M. Ass.* 930, 796.
6. FLOREY, E. W. and MUNO, S. Procedure and apparatus for preservation in lyophilic form of serum and other biological substances. *J. Immunol.* 933, 30-389.
7. GAMBLE, J. L. Extracellular fluid and its kinetides. *Bull. Johns Hopkins Hosp.* 937, 4-61.
8. GOVARTS, P. Osmotic pressure in edema. *Proc. med.* 934, 22-950.
9. Idem. Influence of protein-globulin ratio on osmotic pressure of serum protein. *Compt. rend. Soc. de Biol.* 9-5, 93-443.
10. HARVEY, S. C., and HOWES, E. L. Effect of high protein diet on the edema and growth of fibroblasts in the healing wound. *Ann. Surg.* 930, 9-64.
11. HORMAN, R. L., MASLOWE, E. B. and WINTER, G. H. Blood plasma protein regeneration controlled by diet. *J. Exper. Med.* 934, 59-860.
12. JORANSEN, A. H. Hypoproteinemia. *Acta path. et microbiol. Scand.* 938, suppl. 37 p. 572.
13. JONES, C. M. and EYRON, P. B. Postoperative nutritional edema. *Arch. Surg.* 933, 57-59.
14. KROGH, A. *The Anatomy and Physiology of Capillaries*. 2d. ed. New Haven, 1920.
15. KROGH, A., LUNDG, E. M. and TURNER, A. H. The movement of fluid through the human capillary wall in relation to venous pressure and to the colloidal osmotic pressure of the blood. *J. Clin. Invest.* 932, 63.
16. LEFORS, M. J. Experimental edema produced by plasma protein depletion. *Proc. Soc. Exper. Biol. & Med.* 93-20-38.
17. MANNEN, S. C., NOBBERG, W. A., WARREN, G. S. and WINTER, G. H. Blood plasma protein production as influenced by amino-acids. *J. Exper. Med.* 930, 69-7.
18. MERRAY, P. M. BORDEN, R. P. and RAYCE, I. S. Nutritional edema. Its effect on the gastric emptying time before and after gastric operations. *Surgery* 937, 53.
19. MEINCKE, D. and CORWELL, O. R. The influence of prolonged intensive plasmapheresis upon the ability of the organism to regenerate serum protein. *J. Exper. Med.* 937, 66-403.
20. Idem. The problems of hypoproteinemia. *Yale J. Biol. & Med.* 937, 10-49.
21. MOORE, N. S., and VAN SLIET, D. D. The relationship between the plasma specific gravity, plasma protein content, and edema in nephritis. *J. Clin. Invest.* 933, 8-337.
22. PETER, J. P. Serum Proteins in Disease. *Cycl. Med.* 934, 6-797.
23. POMERANCE, W. J., SLAVEN, H. B., KATZ, D. H. and WINTER, G. H. Plasma protein regeneration controlled by diet. *J. Exper. Med.* 935, 44-56.
24. RAYCE, I. S., STEINER, A. J. and PROHASKA, M. The control of hypoproteinemia in surgical patients. *J. Am. M. Ass.* 940, 14-97.
25. RIGGALL, J. E., STEINER, A. J., RIGGALL, C., CAPOT, F. and FRANK, B. D. Absorption of protein split products from chronic isolated colon loops. *Am. J. Physiol.* 1939, 5-707.
26. SCHADE, H. Quoted by WINTER, S. KILLING, and GOTTSCHE. *Loc. cit.* (34).
27. STARLING, E. H. Absorption of fluids from connective tissue spaces. *J. Physiol.* 305-326, 9-3.



# AN EXPERIMENTAL STUDY OF URETERO-INTESTINAL IMPLANTATION

## IV The Significance of Ureterovesical Reimplantation in the Dog

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**C**LINICAL experience and experimentation on animals have yielded abundant proof of the danger which attends one-stage bilateral uretero-intestinal anastomosis. Implanting the ureter into the large intestine initiates a sequence of pathological changes which commonly result in obstruction of the upper urinary tract and ascending infection. Since both kidneys are affected simultaneously in the one stage operation, these complications are likely to terminate fatally. If one ureter is implanted however and a period of a few weeks is allowed to elapse before the second ureter is transplanted, the kidney on the side of the first operation will have recovered sufficiently from the brunt of the early damage to enhance the possibilities of success.

These facts make it clear that the acid test of any method of uretero-intestinal anastomosis is the result attending the one-stage operation. When a means is found of assuring a uniformly successful outcome following this procedure the hazards of obstruction and ascending infection will have been surmounted and the merit of the operation firmly established. While not justified in human cases, attempts to perfect the one-stage bilateral transplant offer a fertile field for investigation in animals.

It was with a view to appraising the part played by the highly infected nature of the field into which the end of the ureter is implanted in uretero-intestinal anastomosis that a one-stage bilateral ureteroneocystostomy was carried out in 6 dogs. The wall of the bladder is sufficiently similar to that of the

large intestine to make it possible to perform a submucosal ureterovesical reimplantation identical in all respects to a uretero-intestinal anastomosis, the only variable factor being the contamination from the rectosigmoid in the latter procedure.

### EXPERIMENTS

The operations were performed in the following manner. The dog was anesthetized with ether and the peritoneal cavity was entered through a low midline incision. Following exploration of the kidneys, the bladder and lower portion of the ureters were exposed by packing the small intestines into the upper part of the abdomen. The pelvic peritoneum was incised longitudinally at the base of the mesosigmoid and the ureters were freed throughout their lower third.

The left ureter was reimplanted first. It was clamped and divided in its juxtavesical extent and the distal stump was tied off. A site for reimplantation was selected along the lateral wall of the bladder and the area marked with two stay sutures. The detrusor muscle was incised for a distance of 1.5 centimeters between these markers, the edges of the incised muscle being dissected back to expose a diamond-shaped area of submucosa (Fig. 1). Three sutures of 0000 chromic cat gut were then placed from the adventitia of the ureter to the submucosa of the bladder so as to form a triangle at the distal end of the exposed submucosa. A small perforation through the submucosa and mucosa in the center of the triangle was made with the point of a No. 11 blade. After a specimen of urine was aspirated through the opening, the proximal end of the divided ureter was introduced.

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As a part of the study of the destiny of the end of the ureter<sup>1</sup> the end was left long in some instances, short in others. The ureter was anchored by tying the 3 primary sutures (Fig 2A), and the anastomosis was reinforced by uniting the edges of the detrusor muscle over the distal part of the incision with a few interrupted sutures.

The right ureter was reimplanted in a similar manner (Fig 2B) and the abdominal wound was closed without drainage. No attempt was made to extraperitonealize the anastomoses.

The specimen of urine obtained from the bladder in one instance contained pus and gram-positive bacteria (confirmed by culture), the others gave no evidence of infection.

#### RESULTS OF EXPERIMENTS

The animals suffered no apparent ill effects from the operation but continued in excellent health until they were killed—2 at the end of 1 week and the others at 1 month, 2 months, 10 weeks, and 6 months, respectively. The results of the necropsies are summarized in Table I (Fig 3).

<sup>1</sup>An experimental study of uretero-intestinal implantation. V. The destiny of the implanted ureter. (In press)



Fig 1 Ureterovesical reimplantation in the dog. Both ureters are freed throughout their lower third. The left has been divided and its site of reimplantation prepared by an incision down to the submucosa.

In only 2 animals was there evidence of obstruction of the upper urinary tract, a mild bilateral hydro-ureter and hydronephrosis being observed in both dogs killed at 1 week (Fig 3, A and B). A blood non-protein

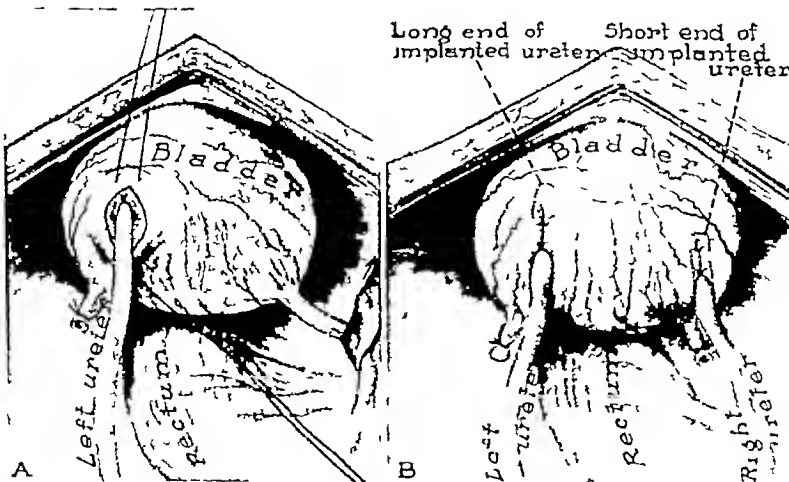


Fig 2 Ureterovesical reimplantation in the dog. A, The end of the left ureter has been inserted through an opening into the cavity of the bladder. It is anchored in place by three sutures joining the submucosa of the bladder to the adventitia of the ureter. B, Both ureters have been reimplanted. The anastomosis is reinforced by sutures uniting the detrusor over the submucosal course of the ureter.



TABLE I.—SERIES OF ONE-STAGE BILATERAL URETEROVESICAL REIMPLANTATIONS IN THE DOG (SEE FIG 3)

No.		Technique bilateral retrovesical reimplantation	Culture of urine (from bladder)*	Sacrificed at	Ascending infection	Obstruc- tion upper tract	Blood PN at surgery stage	Length of end of ureter	Peritonitis	Wound infection
Exp.	Dist.									
A	20	Right: Long end Left: Short end	No growth	week	Mild Mild	Mild Mild	15	cm cm		
B	21	Right: Long end Left: Short end	Gross positive rod.	week	Mild Mild	Mild Mild	45	cm cm		
C	206	Right: Long end Left: Short end	No growth	month			66	cm		Superficial
D	207	Right: Short end Left: Long end	No growth	months	Mild		25			
E	208	Right: Long end Left: Short end	No growth	no week	Mild					
F	203	Right: Short end Left: Long end	No growth	months			66	mm		

\*Obtained at operation

nitrogen at the upper limit of normal in one and a slightly elevated reading in the other gave evidence of mild impairment in renal function. Since these changes were not present in the animals killed later it is reasonable to conclude that they resulted from an early temporary period of partial obstruction in duce by operative trauma.

Examination showed no hyperemia or other gross evidence of inflammation of the ureters or kidneys although, upon microscopic section, a mild bilateral ureteritis and pyelonephritis were observed in the dogs killed at 1 week and a similar unilateral involvement was noted in those sacrificed at 2 months and 10 weeks. This reaction was manifested by an infiltration with leucocytes of parts of the submucosa and adjacent areas of the renal pelvis and ureter (Fig 4). The redundant intravesical end of the ureter sometimes demonstrated a more violent reaction shortly after operation. Although the mucosa, submucosa, and muscularis were almost free from infection the adventitia showed a dense infiltration of polymorphonuclear leucocytes surrounded by an inflammatory debris (Fig 5).

Peritonitis did not occur nor was there any serious wound infection. A superficial supuration of the skin incision developed in one animal.

#### ANALYSIS OF STUDY

It is interesting to note that only the mildest and most transient forms of ascending infection and obstruction occurred following this series of ureterovesical reimplantations. Such findings are in dramatic contrast to the frequency and severity of these complications after uretero-intestinal anastomosis. For example in a typical control series of 6 dogs subjected to bilateral uretero-intestinal anas-

An experimental study of uretero-intestinal anastomosis  
relation of ascending infection to ureteral obstruction (in press)

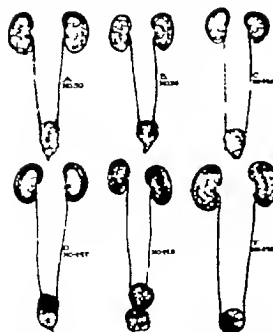


Fig. 3. Changes in the upper urinary tract following bilateral ureterovesical reimplantation (see Table I)



Fig 4 Typical form of ascending infection occasionally observed following ureterovesical reimplantation—mild pyelonephritis is evidenced by a leucocytic infiltration limited to a small area immediately surrounding the renal pelvis Dog killed after 1 week (Right kidney, Dog A, Fig 3, and Table I)

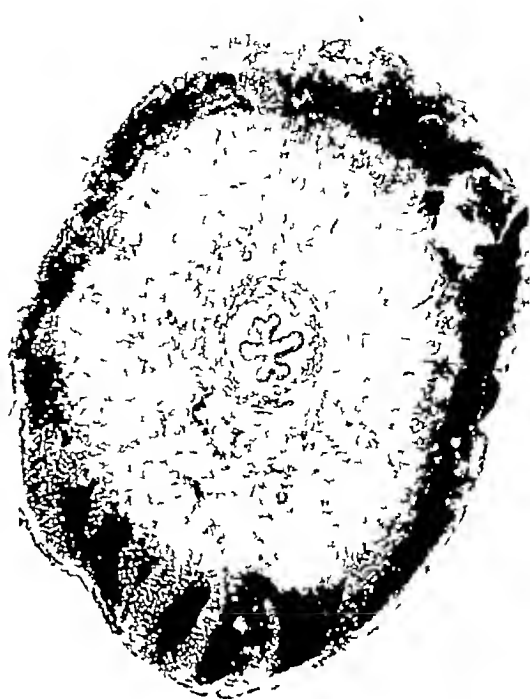


Fig 5 Acute inflammatory reaction surrounding redundant stump of ureter sometimes observed shortly after ureterovesical reimplantation The mucosa, submucosa, and muscularis are scarcely involved, but the adventitia is encased in a zone of inflammatory debris Note the dark clumps of bacteria near the periphery Dog killed at 1 week (Left ureter, Dog A, Fig 3, and Table I)

tomosis, instead of any recession of the early obstructive changes, advanced degrees of late hydronephrosis, hydro-ureter, and severe renal infection resulted (Fig 6) These differences were likewise apparent in another control series in which one ureter was reimplanted into the bladder and the other into the rectosigmoid With an almost uncanny regularity ascending infection and obstruction attended the intestinal transplant while the side reimplanted into the bladder escaped with only the mildest changes (Fig 7) In the two control series the 18 implants into the large intestine progressed to moderate and advanced degrees of obstruction and infection in almost every instance, whereas the 6 reimplantations to the bladder produced only a mild ascending infection and obstruction in one animal (at 6 days), and a mild hydro-

ureter in another (at 6 months) The remainder of the upper tracts were normal following ureterovesical reimplantation except for a hematogenous renal infection observed in the animal killed at 9 weeks

These results permit only one conclusion, that the serious degrees of ascending infection and obstruction are directly attributable to the degree of contamination of the field into which the end of the ureter is introduced

A feature of some encouragement in the ureterovesical reimplantations is that uniformly good results were attained despite the occurrence of mild degrees of infection This finding suggests two important questions as concerns the final conquest of ascending infection and obstruction First, just what degree of infection will be tolerated in the field of implantation without compromising a satisfactory outcome, and, second, is it pos-



Fig. 6. Changes in the upper urinary tract following bilateral uretero-intestinal implantation.

No	Side	Time following operation	Ascending infection	Obstruction
A 30	Right	days	Severe	Mild
	Left		Moderate	Mild
B	Right	days	Moderate	Mild
	Left		Moderate	Mild
C 48	Right	week	Moderate	Mild
	Left		Moderate	Mild
D	Right	month	Moderate	Severe
	Left		Moderate	Severe
E 88	Right	month	Moderate	Moderate
	Left		Moderate	Severe
F 96	Right	months	Severe	Severe
	Left		Severe	Moderate

sible to reduce the degree of infection in the large intestine sufficiently to meet this criterion, whatever it may be, during the post operative period of healing? Following epithelialization of the mucous surfaces of the uretero-intestinal junction and healing by primary union of the other tissues involved in the anastomosis the period of danger is passed. Conditions then correspond to the

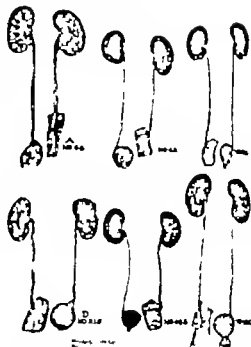


Fig. 7. Changes in the upper urinary tract following ureterovesical reimplantation on one side and uretero-intestinal anastomosis on the other.

No	Site of implant	Time following operation	Ascending infection	Obstruction
A 60	Right, Bladder	days	Mild	Mild
	Left, Intestine		Severe	Moderate
B 43	Right, Bladder	month		
	Left, Intestine		Mild	Moderate
C 76	Right, Intestine	month	Mild	Mild
	Left, Bladder			
D 81	Right, Intestine	6 weeks	Mild	Moderate
	Left, Bladder			
E 130	Right, Bladder	weeks	Focal Nephropathy	
	Left, Intestine		Severe	Severe
F 96	Right, Intestine	months	Moderate	Moderate
	Left, Bladder			

normal arrangement found in some species of animals an arrangement entirely compatible with a normal upper urinary tract.<sup>1</sup>

It would be possible to gain some idea of the amount of infection which is compatible

with satisfactory healing of a ureteral implant by performing a series of reimplantations following graduated contamination of the bladder. It is of more practical interest, however, to investigate the means and effect of reducing the bacteria in the large intestine at the time of uretero-intestinal anastomosis.

Conservative measures, such as a non-residue diet, adequate catharsis, multiple enemas, and the administration of urinary antiseptics have improved the results of the operation, yet they fall short of yielding the final solution to the problem.

The futility of forming an artificial bladder was early demonstrated. While tremendously increasing the operative risk, both the complete and partial exclusion of a part of the large intestine failed in their fundamental purpose, that of providing a sterile reservoir for urine.<sup>1</sup> It was found impossible to sterilize these stagnant urinary pockets, even by frequent irrigation with antiseptic solutions.

In view of these experiences the value of a temporary colostomy in diverting the fecal stream is questionable. Nevertheless, the problem is one of such fundamental importance that it is our purpose to determine to what extent, if any, a temporary colostomy supplemented by irrigations of the distal loop will improve the results of one-stage bilateral uretero-intestinal anastomosis in the dog.

From a clinical standpoint the results would have to be indisputable in order to justify the incorporation of another surgical procedure, if not another stage, to the accomplishment of a uretero-intestinal anastomosis. On the other hand, no effort is too great which would effectively reduce the morbidity and high mortality now exacted by ascending infection and obstruction.

<sup>1</sup>A critical study of the different principles of surgery which have been used in uretero-intestinal implantation. *Tr. Am. Ass. Genito-Urin. Surg.* 1936 pages 15-156 and *Internat. Abstr. Surg.* 1937 313-363.

We are intrigued by still another possibility, less radical than colostomy, but more revolutionary in character. We refer to the possibility of cleansing the mucous surfaces by continuous irrigation of the rectosigmoid. Despite the general policy of delaying lavage until healing is complete there should be no danger of peritonitis, even in the early postoperative days, if the intestine is not overdistended. A continuous current of fluid would remove urine and fecal matter (substances which provide such excellent culture media for bacteria) from around the end of the ureter. This mechanical cleansing should prove more important than any antiseptic quality of the fluid used. If an antiseptic were to be employed for this purpose, poisonous substances should be avoided because of the absorptive activity of the intestine.

#### SUMMARY AND CONCLUSIONS

A one-stage ureterovesical reimplantation was performed in 6 dogs by a technique similar to submucosal uretero-intestinal anastomosis. The only variable factor was the absence of the contaminated field into which the end of the ureter is introduced in the latter operation.

Upon comparing the almost entire absence of ascending infection and obstruction of the upper urinary tract after ureterovesical reimplantations with their common occurrence in uretero-intestinal transplants, one is forced to conclude that serious degrees of these dangerous complications are directly attributable to the overwhelming infection which is present in the large intestine.

It is apparent, therefore, that a line of investigation searching out every possible means of reducing or eliminating infection in the rectosigmoid during the period of healing constitutes one of the key problems to the final perfection of uretero-intestinal anastomosis.

# THE GENESIS OF PEPTIC ULCER IN DOGS FOLLOWING LIGATION OF THE COMMON BILE DUCTS

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SINCE Cruveilhier first described peptic ulcer about a century ago it has been rather generally agreed that the two factors necessary to the production and maintenance of ulcers of the gastric and duodenal mucosa are injury and devitalization of the gastric or duodenal epithelium followed by digestion and continued irritation of the injured area by gastric ferments and acid. Ivy lists mechanical damage, heat, drugs, toxins, peptones, serums, section of the vagus and splanchnic nerves, embolism, thrombosis, anemia, feeding and intravenous injection of specific and nonspecific bacteria, central nervous system lesions, removal of the suprarenal and parathyroid glands as agencies which will cause petechial hemorrhages, superficial hemorrhagic erosion, and acute ulceration. Shore has included localized hemorrhage in the gastric mucosa as a type of injury which may be followed by gastric digestion and ulcer formation. Finally Lipschutz has suggested that

the initial injury to the gastric or duodenal mucosa may be anaphylactic in origin.

Following the initial lesion there are far fewer factors apparently at work, most observers agreeing with Bolton (6) that chronic ulcer originates from the acute lesion, being maintained and healing prevented by the digestive and irritating action of gastric acid. Moynihan however believed that ulcers would exist very often in a diminished and medium and that a high gastric acidity was not essential to ulcer maintenance.

In the dog spontaneous gastric or duodenal ulcers occur but are not common. Turk, in a series of autopsies on 189 healthy and 83 diseased dogs, found no ulcers in the stomach or duodenum. Mann (12) found no lesions of the gastric mucosa in 200 autopsies on normal cats and dogs. Ivy found only 1 acute gastric ulcer in a series of 900 dogs used for laboratory experimentation. Experimental gastric and duodenal ulcers, however, have been reported in dogs by many investigators and due to many causes. Bolton (5) was able to delay the healing of experimental acute ulcers by producing partial pyloric stenosis. Turk produced perforating ulcers of the stomach and duodenum by feeding *Bacillus coli*, and Rosenow could produce them by the intravenous injection of alleged specific streptococci. Durante could produce chronic ulcers by ligating and cutting the splanchnic nerves. Ivy produced ulcers by aseptic embolism with lead chromate but was unsuccessful when finely divided charcoal was used by the same technique. Mann and Williamson (13) were able to produce ulcers in experimental animals by elimination of the secretions normally poured into the gastro-intestinal tract beyond the pylorus. They felt that these ulcers were chemical in character. Following the suggestion of Still and Carlson that gastric ulcers followed a change of gastric motility associated with liver disease Bollman, Staller and

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Fig. Multiple small, spontaneous hemorrhages in the gastric and duodenal mucosa 5 weeks after ligation of the common bile duct. Notice that only one hemorrhagic area near the lower antrum here is ulcerating.



Fig 2 Section of one of the small mucosal hemorrhages in the stomach  $\times 97$



Fig 3 Section of the one ulcer in Figure 1 showing digestion of the hemorrhagic portion of mucosa  $\times 97$

Mann (4) gave cinchophen to dogs in large doses and while most of the animals failed to show demonstrable liver lesions, many did develop areas of ulceration in the gastric or duodenal mucosa. Bollman and Mann (3) produced gastric or duodenal ulcers in about 60 per cent of a group of dogs by ligating the common bile ducts. These, like the Mann-Williamson ulcers, were thought to be due to the absence of alkaline bile with which to neutralize gastric acid.

While the specific etiology of gastric and duodenal ulcers in canines remains as uncertain as it does in human beings there seems to be no question that one of the direct associates of such ulcers is extraduodenal diversion of bile. Kapsinow and Harvey, using a cholecystonephrostomy, produced ulcers in 17 of 43 animals. Berg and Jobling found ulcers in 13 of 23 cases in which a Rous type of fistula was used. Berg felt that the general condition and cachexia of the animals had a definite relationship to ulcer formation but Andrews and Bissell did not find any such direct association between cachexia and ulcer formation. They further concluded that the initial formation of

these ulcers was dependent upon some other factor than acid. In addition, the absence of the neutralizing effects of bile has been shown by Goldman to have little or no effect on the



Fig 4 Sections showing digested and undigested mucosal hemorrhage side by side  $\times 14$



Fig. 5 T large chronic penetrating peptic ulcer

formation of ulcers of the gastro-intestinal tract and while cinchophen will produce ulcers no definite proof has been offered that these lesions are due to liver damage.

In a recent series of 20 dogs, which were being studied for prothrombin changes following ligation of the common ducts, 11 showed gastric or duodenal ulcers at autopsy after icterus of 3 weeks or more. These animals had been fed an especially prepared diet of sucrose cracker meal beef extract salt mixture Fuller's earth and adequate amounts of all the vitamins excepting K and E. They followed the usual course of dogs with obstructive jaundice as described by us (7) and others.

There was no observable variation in the nutrition or appetite of individuals with and without ulcer but at autopsy changes were seen in the gastric mucosa which suggest the bleeding dyscrasia in obstructive jaundice as a background for breaking the continuity of the gastric or duodenal mucosa rather than lack of neutralization of gastric acid or a deficiency state because of acholia and incomplete gastro-intestinal absorption.

Of the 11 animals developing ulcers 9 had gastric lesions, and 2 had ulcers in the duodenum. Of the gastric series only 1 was solitary and the others were either in pairs or multiple. Of the duodenal ulcers, 1 showed two ulcerations while the other had a single ulcer which had perforated into the gall blad-



Fig. 6 Section of upper ulcer in Figure 5 showing perforation through the muscularis mucosae. X 25.

der forming a spontaneous cholecystoduodenostomy.

The genesis of these ulcers was observed through successive changes from early mucosal hemorrhage to complete ulceration and digestion of the mucosa. This series we feel illustrates the cytological steps in ulcer formation and establishes this particular type of gastric and duodenal ulcer as a part of the hemorrhagic diathesis of obstructive jaundice.

*State 1.* Dogs in which the common bile ducts have been ligated begin to develop abnormal bleeding tendencies 3 to 4 weeks after operation. Hemorrhages may occur spontaneously after injury has occurred or following surgery.

In the first instance bleeding may occur from any epithelial surface including the mucosa of the gastro-intestinal tract. These hemorrhages are small to petechial, are of slow oozing character and usually stop spontaneously with repair of the epithelium (Figs. 1 and 2). In the stomach and duodenum the digestive juices attack the part of the mucosa in which the hemorrhage has occurred and, in a small percentage of these areas, the epithelium in its entire depth down to the muscularis mucosae is destroyed. There is at this time little or no inflammatory reaction in these areas (Figs. 3 and 4).

*Stage 2* Once the gastric mucosa is broken such ulceration follows the same course as any other type of gastric or duodenal ulcer with gradual infection of the ulcer crater and cicatrization of the bed. Epithelization is prevented by the constant action of digestive juices, and such ulcers go on to a chronic state with penetration and occasional perforation (Figs 5 and 6)

#### SUMMARY AND CONCLUSIONS

In a series of 20 dogs, following ligation of the common bile ducts, 9 developed gastric and 2 duodenal ulcers 3 to 8 weeks after operation

Such ulcers were started by physiological digestion of spontaneous hemorrhages in the mucosa of the stomach and duodenum which occurred as part of the hemorrhagic diathesis of obstructive jaundice

Once such breaks in the continuity of the mucosa were established, these ulcers followed the same clinical course as others of similar size in the same locations

#### BIBLIOGRAPHY

- 1 ANDREWS, E, and BISSELL, A Soc Exper Biol & Med, 1934, 32 228
- 2 BERG, B N, and JOBLING, J W Arch Surg, 1930, 20 997
- 3 BOLLMAN, J L, and MANN, F C Arch Surg, 1932, 24 126
- 4 BOLLMAN, J L, STALKER, L K, and MANN, F C Arch Int. Med, 1938, 61 119
- 5 BOLTON Proc Roy Soc Lond, 1909, 82 236
- 6 Idem Ulcer of the Stomach Quart J Med, 1911, 5 434
- 7 CARR, J L, and FOOTE, F S Arch Surg, 1934, 29 277-296
- 8 GOLDMAN, LEON J Personal communication
- 9 IVY, A C Arch Int. Med, 1920, 25 6-32
- 10 KAPSNOW, R, EAGLE, L P, and HARVEY, S C Surg, Gynec & Obst, 1924, 39 65
- 11 LIPSCHUTZ, E W The treatment of peptic ulcer based on its etiology—a survey of the systemic causes of the disease. New York M J & Rec, 1928, Dec 19, pp 630-633
- 12 MANN, F C J Exper Med, 1916, 23 203
- 13 MANN, F C, and WILLIAMSON, C S Ann Surg, 1923, 77 409-422
- 14 MOYNIHAN, SIR BERKELEY Two Lectures on Gastric and Duodenal Ulcer New York Wm Wood & Co, 1923
- 15 SHORE, B J Acute ulcerations of the stomach in children Ann Surg, 1930, 92 234-240
- 16 STILL, K S, and CARLSON, A J Am J Phys, 1929, 89 34
- 17 TURCK, F B J Am. M Ass, 1916, 67 1784



# THE CLINICAL VALUE OF THE SERUM AMYLASE TEST

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THE significance of the serum amylase determination as a valuable and reliable diagnostic aid has long been the subject of considerable clinical uncertainty. Tests of biliary and kidney function have been so profitable that a similar usefulness seemed possible in the diagnosis of deceptive pancreatic disease. From a review of the literature regarding amylase there appears to exist noteworthy disagreement and lack of experimental uniformity which might readily nurture seeds of clinical caution and doubt. However recent investigators have rather successfully challenged some of these discrepancies and qualified certain other discordant results as being more apparent than real. Technical variation has inevitably been responsible for some dissension among observers yet, if serum amylase values are regarded only with comparative and not quantitative accuracy their reliability assumes a new importance and may well satisfy a most helpful diagnostic rôle. A lack of ultimate quantitative precision should not impugn the clinical value of the serum amylase test. It is of more genuine diagnostic importance to determine the deviation from the normal amylase limit than to ponder the significance of some isolated unit of activity.

Conflicting results and disagreement among competent authors have been generally attributed to a difference in the methods of investigation and to the confusing arbitrary units and intangible values used to express amylase activity. Fundamentally the subject is a most complicated one and fraught with many perplexing physicochemical problems, yet its clinical application is simple and readily carried out. The basic need for a proper standardization of optimum hydrogen ion concentration, electrolyte content, temperature amount of substrate, and reaction time has been fully realized by Davison (1925) Elman

and McCaughan (1927) Muhlfield (1928), Meyers and Reid (1933) Schmidt, Greenwald and Ivy (1934) Somogyi (1938) and others. Although a final correlation and evaluation of this quantitative chemical data regarding amylase cannot be made at present, a plan of procedure has been outlined and further investigation should considerably enhance the development of the kinetics of enzyme chemistry.

In 1833 Payen and Pernoix first precipitated a starch-splitting product from malt which they named diastase. Magendie (1846) noted the presence of a ferment in the blood capable of changing starch to sugar. By injecting starch intravenously he found that after 10 minutes the blood no longer gave a starch-iodine reaction, but that the content of blood sugar had increased considerably. Claude Bernard, préparateur to the master Magendie at the Collège de France was an eminent contributor to the study of sugar metabolism and the rôle of pancreatic juice in the process of digestion. In 1849 his studies led him to believe that the action of pancreatic juice upon starch was not a special property of that organ alone, but that saliva and blood serum also had a similar amylolytic activity. Foster (1866-67) found amylase<sup>1</sup> widely distributed in the animal body and by noting the time required for the conversion of a given quantity of starch, roughly determined the amount of ferment present. He observed that the blood and urine amylase of six diabetic patients in no way exceeded that found normally.

Carlson and Luckhardt (1908-09) in reviewing the more important contributions to the subject, pointed out that Bainbridge and Beddard (1907) found no disappearance of blood amylase following pancreatectomy in cats. Schlesinger (1908) on the contrary extirpated the pancreas in two dogs and one cat and reported the complete disappearance

<sup>1</sup>The terms *amylase* and *diastase* are used synonymously by most authors. If prefer the more descriptive term *amylase* and in this paper will use it exclusively.

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Amylolytic activity has been measured by two general types of indirect methods. One has been based upon the activity of the enzyme in the breaking down and disappearance of starch and the other on the accumulation of a reducing sugar formed by the enzymatic hydrolysis of starch. Stringent objections have been indicated in both categories. Using the first of these principles Wohlgemuth (1908) determined the amylolytic activity of serum by the addition of iodine to a starch substrate thus making a colorimetric comparison possible. As the reaction progressed the starch was converted to erythro-dextrin, achroodextrin, maltose and, perhaps, glucose. The point at which the violet color yields to the brownish red of erythro-dextrin is usually the end point adopted. Somogyi (1938) and others have pointed out the inherent vulnerability of this procedure—its difficulty in the selection of an end point, its lack of standardization, its time and materials consumed, and, finally its untrustworthiness. Meyers and Reid (1933) report a plus or minus 25 per cent error in the employment of this method of procedure.

Following the ingenious work of Northrop and Hussey (1922-23) Davison (1925) and Elman and McCaughan (1927) took advantage of the fact that the viscosity of solutions decreases as the molecules dissolved in them are hydrolyzed into smaller and smaller units. Amylase activity could thus be measured by the decrease in viscosity of starch paste. The unique merits and sundry advantages of this mode of analysis cannot be gainsaid, yet the method has been found to contain a measurable source of error—namely mixed aggregates of starch and serum protein are formed by adsorption and tend to separate out and form a sediment, resulting in a diminished viscosity. Although the nature of this inaccuracy is said to be most marked with low amylase values, nevertheless studies making use of this method must be carefully scrutinized and confirmed by a more acceptable procedure. A systematic study of enzyme activity by present polarimetric, spectroscopic, or other physicochemical means has found a limited field of usefulness outside of the experimental laboratory.

Amylase estimation by various sugar reduction methods, on the contrary, has found much favor in the literature of the last 25 years. A critical comparison of these methods and their practical application for general use has been the object of several recent important investigations. A review of this work is not within the scope of the present paper. It may be said, however, that in the cascade of amylolytic reactions starting with starch and ending in sugar production there are many obscure factors whose influence remains unknown. The velocity of enzyme activity toward different parts of the cascade is not known. The presence of activators or inhibitors as side products has not been definitely ascertained. The formation of a reducing sugar (principally maltose) may occur before much of the starch has disappeared or conversely all of the starch may be converted to dextrin before any sugar is formed. Several analytical methods compute their results on the basis of a glucose standard whereas mostly, the reducing sugar formed by amylolytic activity is maltose.

Thus, even a cursory appraisal makes it quite apparent that there may exist many conspicuous sources of error among the several sugar reduction modes of analysis. As previously suggested standardization of technique will undoubtedly result in more uniform amylase values and a more fundamental basis for their interpretation. Perhaps precise quantitative accuracy will be achieved only when a more direct means of enzyme isolation is created. Meanwhile the very lack of sensitivity to serum amylase changes in diseases other than pancreatitis may be the essence of its diagnostic value in that disease.

The method employed in this investigation was first conceived in principle by McClure, Wetmore, and Reynolds (1921) and is based upon the determination of the reducing sugar formed in the enzymatic hydrolysis of starch by a modification of the Folin Wu technique. In the preparation of the reagents and the analytical procedure, however, we have observed the standards employed by Somogyi (1938) and the substitution of the Folin and Wu method for the more complicated, although

Detailed description of the method of analysis may be found in Somogyi's paper. The method of Folin and Wu is described in J. Biol. Chem. 1906, 41: 207; Ibid. 1906, 67: 371; Ibid. 1906, 82: 83.

TABLE I—AGE

Patient	Under 25 mgm %	25-50 mgm %	Over 50 mgm %
1	58	80	52
2	46	75	117
3	63	52	100
4	82	100	74
5	45	91	119
6	80	105	59
7	102	86	46
8	77	119	91
9	71	98	101
10	88	49	61
Average serum amylase	71	86	82

TABLE II—AMYLASE VALUES IN COMPARISON  
WITH CLINICAL FINDINGS—25 FEMALES,  
25 MALES

Female		Male	
Diagnosis	Amylase mgm %	Diagnosis	Amylase mgm %
Normal	52	Normal	75
Normal	113	Normal	113
Normal	80	Normal	91
Normal	71	Normal	80
Deaf	52	Normal	61
Peptic ulcer	40	Peptic ulcer	89
Peptic ulcer	84	Peptic ulcer	49
Peptic ulcer	67	Peptic ulcer	83
Malnutrition	74	Malnutrition	95
Hemorrhoids	50	Hemorrhoids	49
Dermatitis	62	Dermatitis	54
Hodgkin's	82	Hodgkin's	113
Tuberculosis	82	Tuberculosis	105
Pneumonia	60	Pneumonia	50
Pneumonia	71	Pneumonia	96
Hernia	74	Hernia	115
Hernia	91	Hernia	83
Hernia	60	Hernia	111
Colon cancer	50	Rectal cancer	49
Cervical cancer	72	Lung cancer	102
Breast cancer	74	Stomach cancer	73
Appendicitis	69	Appendicitis	95
Appendicitis	110	Appendicitis	63
Syphilis	85	Syphilis	56
Heart disease	61	Heart disease	58
Average serum amylase	76	Average	81

more accurate, Shaffer-Hartmann technique was the single change that we felt justified in making. A carefully prepared 15 per cent starch paste was used which, by repeated test, conformed to the optimum hydrogen-ion requirement of 6.972. The starch paste was freshly prepared every 2 weeks. This precaution must not be underemphasized as it eliminates the possibility of bacterial breakdown of the starch, or the hydrolysis associated with repeated boiling. A large amount of starch is made up at one time and may be kept in a desiccator as a powder indefinitely. Thirty minutes' incubation in a water bath at 40 degrees C was the standard time and temperature adopted. The entire procedure in both materials and method is simple and may be expediently performed in less than 1 hour. The results of amylase activity are expressed in milligrams of reducing substance per 100 cubic centimeters of serum, and values are consistently reliable up to five times the limits of normal. Saline dilution of the serum allows for determining higher values. A control blood sugar must be determined and deducted from the total reducing substance of the serum, as it is only the difference which represents amylase activity. In our experience normal values were found to range from 40 to 175 milligrams of reducing substance per 100 cubic centimeters of serum (mgm per cent), with some slight variation beyond either limit. Lipase determinations were performed according to a modification of the Loevenhardt method as used by Cherry and Crandall (1932) and Comfort and Osterberg (1934).

#### RESULTS

Although the analytical procedure employed in this investigation is open to much the same

criticism applied to all sugar reduction methods, yet, under carefully controlled conditions, practical experience with 1500 serum amylase determinations has minimized our sources of error and justified our confidence in the reliable nature of these results *per se*. However, the interpretation and application of these records to clinical conditions remain a matter of continued correlated study and medical judgment.

*Duplicate series.* A series of 20 representative serum amylase values was determined in duplicate and an average of plus or minus 7 per cent error was found to be present. The greatest deviation was 11 per cent and the smallest was zero. This degree of error is of no practical consequence and may be attributed to variations in laboratory technique.

*Age.* Table I represents the serum amylase values in a group of normal persons and clinic patients in which there was no reason to suspect an abnormal serum amylase level. These 30 individuals included both sexes and were unselected except for age. It would appear from these three categories that age

TABLE III.—SERUM AMYLASE ACTIVITY IN 720 PATIENTS WITH DIVERSE DISEASES

Condition	Serum amylase values						Total Patients	Avg Amylase level
	Normal 40-72 mgm %		High 72-87 mgm %		Low 88-98 mgm %			
	Number of patients	Number of Amylase tests	Number of patients	Number of Amylase tests	Number of patients	Number of Amylase tests		
Normal	18						18	94
Appendicitis	46	53					96	104
Cachectic-vascular diseases	67	76			6			73
Diabetes	24	24			6	20	30	
Gastro-intestinal diseases	79						79	75
Gastro-urinary diseases	93	104					93	104
Gynecological diseases	25	53						
Hernia	45	66					47	23
Infectious mononucleosis	3			15			6	100
Kempatic diseases	6	70					64	97
Peptic ulcer		49						200
Pilonidal sinus		12						21
Pneumonia	16	18					30	20
Pregnancy								20
Rectal diseases	72						72	97
Rheumatic fever	72						12	77
Syphilis								20
Thyroid diseases	20	67					20	20
Tuberculosis								20
Macroadenoma	12	181					17	20
							720	97

has relatively little effect upon amylase values. In general it was found that infants had a lower range of amylase activity than adults however although the individual variation in both was wide it remained within normal limits.

**Ser.** Average amylase values in a parallel group of 25 males and 25 females with comparable clinical conditions (Table II) were found to be approximately the same. The specimens used were from unselected patients in which all amylase values were within normal limits. Marked obesity in females was noted to be associated with a lowered amylase activity.

**Clinical condition.** In Table III there is listed the serum amylase activity of 720 patients with many diverse diseases which, for the most part cause no serious alteration in amylase level. A few values may rise above the limits of normal and others tend to fall

below. In the majority of these instances, however repeated tests within 24 hours reveal a prompt return to normal with no subsequent aberration. We have been unable to account for these isolated spontaneous, and transient rises in serum amylase although Friedman and Thompson (1936) have found similar elevations to occur in experimental dogs. These investigators attribute the altered amylase activity to either a functional or pathological pancreatic response. Clinically spontaneous changes seem to bear no relation to food, drugs, temperature elevation, leucocytosis, or pain. Several amylase rises have been noted directly to follow laparotomy. It may be presumed that the intra-abdominal handling of the pancreas or perhaps the effect of the anesthesia was responsible but we have no evidence in support of these contentions. In a small series of amylase determinations performed shortly after biliary tract operations,

TABLE IV—SERUM AMYLASE VALUES IN 99 CASES OF GALL-BLADDER DISEASE

	Number of patients	Average amylase on admission mgm. %
Acute and subacute		
Cholecystitis	26	69
Cholecystitis and cholelithiasis	18	67
Chronic		
Cholecystitis	17	75
Cholecystitis and cholelithiasis	22	93
Choledocholithiasis	16	67

there was no constant irregularity observed. The striking expression of normal amylase levels in 94 per cent of 720 patients is a rather convincing manifestation of its stability in diseases other than pancreatitis.

*Appendicitis* Among 50 patients operated upon for acute appendicitis 4 had elevated amylase values and the remainder were normal. In 2 of these patients with high levels the appendix was found to be normal by pathological examination. One may speculate as to whether a mild edematous and transient pancreatitis could be diagnostically confused with appendicitis.

*Cardiovascular disease* Seventy-four patients with cardiovascular disease of varying degree were investigated. Six patients were noted as having a lowered serum amylase, and the remainder except for one to be normal. All 6 of those patients with a decreased amylase level were in severe congestive heart failure. The rôle of visceral stasis and liver and pancreatic engorgement in decreasing amylase activity has not been clearly defined, yet in studying patients with an impaired liver function we believe that such an association is in all probability more than just incidental.

*Diabetes* Among 40 cases of diabetes that were observed there were both insulin treated and untreated patients. The amylase activity was depressed in 6 cases. The blood sugar levels in these particular patients were not exceptionally high, although from our records there appears to exist an inverse ratio between the blood sugar and the serum amylase. This may best be seen by a comparison of the blood sugar and serum amylase values in patients with a marked hyperglycemia.

TABLE V—BLOOD SUGAR AND SERUM AMYLASE IN MARKED HYPERGLYCEMIA

Patient	Blood sugar	Serum amylase
1	222	102
2	268	42
3	286	47
4	236	50
5	222	100
6	236	94
7	250	60
8	400	35
9	286	34

Is the same process which apparently impairs the internal secretory function of the pancreas in diabetes also responsible for its influence upon the so called external secretory function?

*Genito-urinary diseases* Ninety-eight patients with diverse genito-urinary diseases were studied in this investigation. In 4 cases the amylase was elevated and in 2 it was lowered. Terminal uremia was present in 2 of the patients having increased amylase values. Although it is generally known that amylase is excreted by the kidney, we were unable to correlate any constant serum amylase change with decreased kidney function as indicated by a moderate retention of nitrogenous products.

*Gynecological disease* A mild but persistent increase in serum amylase activity was noted in 1 patient treated surgically and found to have a ruptured graafian follicle. The remaining gamut of gynecological conditions, including ovarian disease, failed to manifest any abnormal amylase values.

*Infectious mononucleosis* A striking case of infectious mononucleosis was observed in which a persistent elevation of serum amylase was noted in 18 determinations over a period of 4 weeks. Following the patient's clinical recovery there was no inclination of the serum amylase to return to normal. Five additional cases of infectious mononucleosis showed no such aberration.

*Peptic ulcer* Twenty-three patients with peptic ulcer were found to have normal amylase levels. Two patients were observed to have high amylase values. The first of these was a case of an acute ulcer perforating into the head of the pancreas. Probstein, Gray, and Wheeler (1938) have recently re-empha-

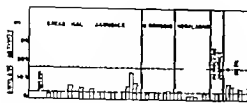


Fig. 1. Sixteen patients with liver disease showing depressed amylase activity.

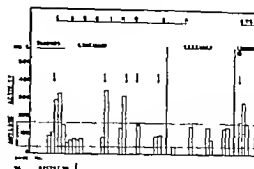


Fig. 2. The serum amylase values in 10 patients with pancreatic tumors. The pre-operative level was normal in all cases except one.

sized the association of such ulcers with increased serum amylase values and reported 4 cases in which a localized pancreatitis resulted from the perforation. Two patients in our series had a frank ruptured ulcer with out involvement of the pancreas, and in both the amylase remained within normal limits.

The second patient with an elevated amylase had a chronic stenosing ulcer and a gastric resection was performed. The duodenal stump was buttressed against the pancreas. Following this procedure the patient's early postoperative course was marked by severe vomiting and epigastric pain. The serum amylase which had hitherto been normal was now found to be elevated. Many observers have called attention to the danger of pancreatitis following gastric resection in which the pancreas is traumatized or otherwise injured by operative manipulation.

**Thyroid disease.** Disease of the thyroid gland produced relatively little effect upon amylase activity. No correlation could be drawn between the basal metabolic rate and the amylase level.

**Miscellaneous.** Minor deviations from the normal amylase level rarely occurred in a great diversity of clinical conditions. The interpretation of these isolated results was impossible. We regret that in this investigation we were unable to study patients with psychiatric, neurological or neurosurgical disorders.

#### MUMPS

Thirteen cases of mumps were observed in this study: 12 of epidemic mumps and 1 of surgical mumps. In concomitant serum amylase and serum lipase studies all lipase levels

were normal whereas the amylase was considerably elevated in practically all patients except those in whom the parotitis was unusually mild or the determination made late in the course of the disease. Orchitis and encephalitis as complications of mumps produced no effect upon the activity of these enzymes. Pancreatitis complicating mumps was not present in the diagnoses of this group. Two cases of salivary gland cysts both had normal amylase values.

#### DISEASES OF THE LIVER

Diseases of the liver regardless of kind appear to have a depressing effect upon serum amylase activity (Fig. 1). Sixteen patients with diverse diseases of the liver were subjected to investigation. Jaundice was the striking clinical feature in this group of cases. The diagnosis was confirmed by operation or autopsy in all of those patients having cirrhosis of the liver or hepatic neoplasms. In the neoplastic group 1 patient had a metastatic melanosisarcoma and 2 patients had metastatic carcinomas: 1 from the gall bladder and the other from the rectum. Patient 15 in Figure 1 entered the hospital almost moribund with a severe yellow atrophy of the liver. The diagnosis was confirmed by postmortem examination yet two serum amylase values taken just before death remained within normal limits.

#### TUMORS OF THE PANCREAS

Nine patients with carcinoma of the pancreas were observed in this study (Fig. 2). In 5 cases the diagnosis was confirmed at

either operation or autopsy and in the diagnosis was presumptive. The pre-operative amylase levels were normal in all cases except 1, patient 3, Figure 2, and in this exception a laparotomy revealed an extensive carcinoma surrounded by areas of pancreatitis and fat necrosis. Patient 1 (Fig 2) had a carcinoma of the ampulla of Vater which was resected. It is significant to note the normal pre-operative amylase level in those cases in which a tumor was resected or a biopsy taken, whereas the postoperative amylase level incident to the operative pancreatic trauma showed a marked and immediate elevation.

Apparently the slow growth of a pancreatic neoplasm is unlikely to produce the elevated amylase level so commonly associated with more sudden ductal obstruction, hemorrhage, or inflammation. Similarly, the acinar atrophy resulting from the pressure and invasion of pancreatic tumors is not sufficient to cause a striking fall in serum amylase.

One patient with a pancreatic cyst was observed after operation. An elevation of amylase occurred on one occasion shortly after operation. The results of amylase determination in this particular group of cases closely parallels a larger series of patients with pancreatic tumors and cysts reported by Wakefield, McCaughan, and McVicar (1930).

#### GALL-BLADDER DISEASE

Ninety-nine patients with gall-bladder disease were carefully studied both before and after operation. Table IV represents the average serum amylase values which in all categories fell within the range of low normal. However, each individual patient presented a wide amplitude of amylase variation particularly when followed for a long period of time. Thus, the interpretation of individual values must be undertaken separately if we are not to be misled by the fallacy of average statistics.

More clearly to define this position, the following histories outline the amylase level in 3 illustrative cases of gall-bladder disease.

Patient 1 entered the hospital because of chronic cholecystitis and cholelithiasis, a diagnosis made by her family physician. While in the course of pre-operative preparation the patient developed unmistakable signs and

symptoms of common duct obstruction. At this time the amylase, which had hitherto been normal, increased decidedly. Shortly thereafter the patient was operated upon and a large stone was found impacted at the ampulla of Vater. Following its removal the patient's rapid clinical convalescence went hand in hand with a return to normal amylase activity.

Patient 2 had a subacute cholecystitis and cholelithiasis with normal amylase activity. At the time of operation a rather large calibered and long limbed T-tube was placed in the common duct. The serum amylase rose sharply and remained elevated until the T-tube was removed 2 weeks later. It is suggestive that the descending limb of the T-tube may have impinged upon the duct of Wirsung or, by edema, occluded it, thus causing pancreatic obstruction and a concomitant rise in amylase.

Patient 3 had an uneventful postcholecystectomy convalescence until the fourth day after operation. At this time the patient's temperature rose, jaundice was noted, pain was present, and large amounts of bile commenced to discharge from the wound. The serum amylase which had been normal on several previous determinations now rose sharply. The amylase activity of the draining bile, which is normally very low, increased markedly. Within a day or two the patient's condition was distinctly improved, however, and the amylase level of both the serum and the bile returned to normal. Shortly thereafter a small cholesterol-bilirubin stone was found in the stools which probably was responsible for the obstruction to both the common and the pancreatic ducts at the ampulla of Vater.

The important studies of Millbourn (1936), Foged (1933-34), Branch and Zollinger (1938), and others have all pointed out that essentially the rise of serum amylase in gall-bladder disease depends upon the location of the stone and the anatomical interrelations of the bile and pancreatic ducts. It has been our experience that such amylase elevations are only of a moderate amplitude and are seldom to be confused with the increased amylase activity noted during the onset of acute pancreatic necrosis. Gall-bladder disease without com-



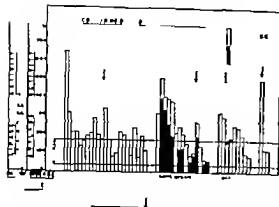


Fig. 3. The serum amylase and serum lipase activity of 4 confirmed cases of acute pancreatitis. The highest level occurs early in the course of the disease.

non-duct stones rarely gives abnormal amylase values

#### ACUTE PANCREATITIS

Four patients with acute pancreatitis, the diagnosis confirmed at operation, were observed in this investigation. The amylase activity in all of these cases (Fig. 3) and the lipase activity in at least one of them were intensely increased. Concomitant urinary amylase determinations were found to have a greater range of daily fluctuation but in general, to corroborate the serum amylase level. A lag of 24 hours was frequently noted in the urinary amylase value when compared to that of the serum amylase.

The serum amylase response reaches its peak within the first 48 hours of the disease and may fall rapidly if not precipitously within the next few days. Thus, the diagnostic value of the amylase test is limited to the early course of the disease but it is precisely at this time that it is of greatest benefit in the differential diagnosis of the acute abdomen. Practically all observers agree that significant serum amylase elevations occur regardless of the nature or severity of the pancreatic lesion. In our investigation patients 2 and 3 represented the milder acute edematous type of pancreatitis, whereas patients 1 and 4 were representative of the more fulminating forms of acute pancreatic necrosis; however a marked serum amylase rise was present in both groups of patients.

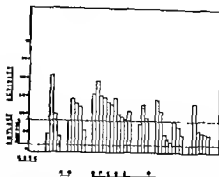


Fig. 4. Six patients in whom the serum amylase values were increased. The clinical diagnoses are in doubt although presumably opinion based upon amylase studies favored pancreatic involvement.

Patient 1 (Fig. 3) suffered a prolonged period of retarded convalescence which was more or less indicated by the fluctuating postoperative amylase values. Dragstedt, Haymond and Ellis (1934) have called attention to this condition of pancreatic cachexia, probably the result of extensive damage to the pancreas, and have suggested substitution therapy—particularly the internal secretory enzyme lipocalc. The rapidity with which the serum amylase level returns to normal in cases of acute pancreatitis may serve as a presumptive prognostic sign in predicting the extent of pancreatic destruction.

The secondary rise in serum amylase following operation (Fig. 3) appears to have been the result of surgical manipulation and maneuvers designed to insure pancreatic decompression. Principles of pancreatic apposition based upon surgical therapeutic procedures are not founded upon the exact anatomical consideration of the pancreatic capsule and its lobular extension. The more general acceptance of the serum amylase test as a reliable aid in the diagnosis of acute pancreatitis has in part been responsible for the recent tendency to treat this disease conservatively.

In our limited experience with the serum lipase test we have noted that its activity parallels that of the serum amylase in all of the pancreatic diseases. Its aptness to remain elevated for a longer time has been noted by others but the fact that its performance takes 24 hours seriously handicaps its practical usefulness in clinical emergencies.

## BILIARY TRACT DISEASE

The unconfirmed diagnoses of the patients represented in Figure 4 varied from post-cholecystectomy syndrome and biliary dyskinesia to pancreatic reflux and chronic pancreatitis. From the clinical history and amylase studies of these patients it is not unlikely that the responsible locus might very well have been a pancreatic lesion. The experimental work of Archibald (1919) and Wangenstein, Leven, and Manson (1931) supports the opinion that transient states of pancreatitis may be produced by pancreatic reflux in the course of a disturbance of the normal function of the sphincter of Oddi. The investigations of Cole (1938) and Elman (1937) add clinical confirmation to this conception and reaffirm the diagnostic value of the serum amylase test in acute edematous pancreatitis. The obscurity of the clinical signs and symptoms in this group of cases constitutes a diagnostic hazard, and, were it not for enzyme determinations, many patients with acute edematous or interstitial pancreatitis might continue to be clinically unrecognized.

## CONCLUSIONS

- 1 Age, gender, diet, vitamin deficiency, and starvation have practically no effect upon serum amylase values
- 2 Normal serum amylase levels range within constant limits when determined by a reliable method of analysis
- 3 Because of the indiscriminate chemical composition and enzyme concentration in urine, feces, and duodenal contents, amylase activity under such conditions is less uniform and, so, as a diagnostic aid less trustworthy
- 4 Ninety-four per cent of 720 patients having clinical conditions other than mumps or diseases of the biliary system were found to have normal serum amylase values
- 5 Patients with mumps were observed to have elevated amylase levels
- 6 Patients with liver disease, regardless of kind, often have depressed amylase activity
- 7 Deviation from normal amylase values occurs infrequently in diseases other than pancreatitis. The range of this aberration is rather restricted and unlikely to be a source of diagnostic confusion

8 A prompt and significant rise in serum amylase activity occurred in 4 cases of acute pancreatitis in which the diagnosis was confirmed and in 6 similar cases in which the diagnosis was presumptive. The amylase elevation reaches its peak within the first 48 hours of the disease and usually returns to normal several days thereafter.

9 The serum amylase determination is a most helpful and reliable aid in the diagnosis of acute pancreatitis, particularly if this disease is to be treated conservatively.

I am most grateful to Dr. H. Stine and Miss Weinreb for their laboratory assistance and to Dr. E. Fishberg for her helpful interest and counsel.

## BIBLIOGRAPHY

- 1 ARCHIBALD, E. Experimental production of pancreatitis in animals as result of resistance of common duct sphincter. *Surg, Gynec & Obst*, 1919, 28 529
- 2 BAINBRIDGE, I. A., and BEDDARD, A. P. *Biochem J*, 1907, 2 89
- 3 BERNARD, CLAUDE. Du suc pancréatique et de son rôle dans les phénomènes de la digestion. *Arch gén de méd*, 1849, 19 60-81
- 4 BRANCH, C. D., and ZOLLINGER, R. Value of blood diastase in diagnosis of common duct stone. *Am J Surg*, 1938, 41 233-237
- 5 CARLSON, A. J., and LUCKHARDT, A. B. On the diastases in the blood and the body fluid. *Am J Physiol*, 1908, 23 148
- 6 CHERRY, I. S., and CRANDALL, L. A., Jr. Specificity of pancreatic lipase: its appearance in blood after pancreatic injury. *Am J Physiol*, 1932, 100 266-273
- 7 COLE, W. H. Treatment of acute pancreatitis, Collective review. *Internat Abstr Surg*, 1938, 67 31-38
- 8 COMFORT, M. W. Tests of pancreatic function. *J Am M Ass*, 1940, 115 204-2050
- 9 COMFORT, M. W., and OSTERBERG, A. E. Lipase and esterase in blood serum. *Proc Staff Meet Mayo Clin*, 1934, 9 250
- 10 DAVISON, W. C. *Bull Johns Hopkins Hosp*, 1925, 37 281
- 11 DIAMOND, J. S., and SIEGEL, S. A. The secretion test in the diagnosis of pancreatic diseases with a report of 130 tests. *Am J Digest Dis*, 1940, 7 435-442
- 12 DRAGSTEDT, L. R., HAYMOND, M. E., and ELLIS, J. C. Pathogenesis of acute pancreatitis (acute pancreatic necrosis). *Arch Surg*, 1934, 28 232-291
- 13 ELMAN, R. Variation of blood amylase during acute transient disease of the pancreas. *Ann Surg*, 1937, 105 379-384
- 14 ELMAN, R., ARNESON, N., and GRAHAM, E. A. Value of amylase estimations in diagnosis of pancreatic disease, clinical study. *Arch Surg*, 1929, 19 943-967
- 15 ELMAN, R., and MCCAUGHAN, J. M. Quantitative determination of blood amylase with viscosimeter. *Arch Int Med*, 1927, 40 58-64
- 16 FOGED, J. The chemical significance of diastasuria. *Acta chirurg Scand*, 1933-34, 73 203-218

7. FOSTER, M. JR. Notes on amylolytic ferment. *J Anat. & Physiol.* 366-67, 97-3.
8. FRIEDMAN, I. and THOMPSON, W. R. Induced and spontaneous changes in blood amylase, particularly in relationship to the pancreas, experimental study. *Ann. Surg.* 936, 94 383-402.
9. HENRY, R. G., and LOWMEYER, J. H. *J Gen Physiol.* 9, 4 355.
10. KAUFMAN, M. *Compt. rend. Soc. de Biol.* 894, 46 30.
11. LIPPET, R., and BARR, T. M. *Compt. rend. Acad. d. sc.* 89, 3 729.
12. MACARTHUR, F. *Compt. rend. Soc. de Biol.* 896, 3 89.
13. McCLEURE, C. W. WELSH, A. S., and REYNOLDS, L. New methods for estimating enzymatic activities of duodenal contents of normal man. *Arch. Int. Med.* 93, 27 706-75.
14. MERRILL, V. C., and REED, E. Comparison of several different methods for the quantitative estimation of diastase. *J Biol. Chem.* 933, 99. 503-605.
15. MILLBROOK, E. On diastaseuria conditions in cases of jaundice due to cholelithiasis, acute hepatitis, and malignant tumors. *Acta chirurg. Scand.* 936 77 523-55.
16. MURFIELD, M. Experiments on blood amylase. *Columbia Univ. Dissert.* 9 &.
17. P. VETZ and PRIEOR. Mémoire sur la diastase les principaux produits de ses réactions et leurs applications aux arts industriels. *Ann. de chim. et phys.* 333, 33 73.
18. PROBERT, J. C. WICKELER, P. A. and GR. S. H. Perforated peptic ulcer: differentiation from acute pancreatitis by diastase determination. *J Lab. & Clin. Med.* 939, 34 449-452.
19. SCHLESINGER, W. *Deutsche med. Wochenschr.* 1908, 34 503.
20. SCHUBERT, C. R., GREENGLASS, H. and IVEY, A. C. Comparison of methods for quantitative estimation of diastase in duodenal fluid. *Am. J. Digest. Dis.* 934, 8 8-677.
21. SONOGUTI, M. Micro-methods for the estimation of diastase. *J Biol. Chem.* 934, 5 399-44.
22. WATKINS, E. G., McCARTHY, J. M. and McCARTHY, C. S. Amylase in salivary and in chronic pancreatic diseases. *Arch. Int. Med.* 930, 45 473-478.
23. WARMUTH, O. H. LUTHER, L. and MANSON, M. Acute pancreatitis. Experimental and clinical study with special reference to significance of biliary tract factor. *Arch. Surg.* 93, 3 47-73.
24. WOLFGUT, J. Ueber eine neue Methode zur quantitativen Bestimmung des diastatischen Ferments. *Biochem. Ztschr.* 903, 9.
25. WOLFGUT, J. *Biochem. Ztschr.* 909, 35.

# CANCER OF THE RECTUM AND RECTOSIGMOID

## Its Surgical Treatment

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THE *annals of medical history* record many and varied procedures of diagnosis and treatment for cancer of the rectum. Historical data on surgery as far back as the Hippocratic era mention rectal operations. True, most of these procedures were for fistulas or hemorrhoids but occasionally one reads of cauterization operations for tumors which obviously were malignant. Beginning with these primitive maneuvers surgery for rectal cancer steadily progressed from local operations to abdominal drainage procedures and finally to a combination of colostomy and removal of the rectum which culminated in the modern combined abdominoperineal operation in one and two stages.

A brief review of some of these historical data which mark this evolution is interesting and is put down here in the belief that one should not lose sight of the efforts of pioneer surgeons in the present day atmosphere of standardization.

Surgical intervention for cancer of the rectum was first proposed by Morgagni at the beginning of the eighteenth century, but not until 1739 was the initial operation, a form of posterior proctectomy, undertaken by Faget.

It was not until nearly 100 years later that the procedure was again attempted by Lisfranc, who in 1826 performed his first successful posterior resection for carcinoma of the rectum. In 1829 his pupil, Pinault, published a thesis in which he reported 9 cases and, therefore, credit is usually given Lisfranc for laying the foundation of radical surgical removal of the rectum for cancer. Be that as it may, these early procedures were pitifully inadequate, for during this period the operation was merely a circular amputation of the anal canal leaving a troublesome incontinent perineal anus, and as we now know from a slow and painful accumulation of 200 years' experience, a fertile field for early recurrence in the bountiful supply of regional lymphatics.

Diefenbach and Velpeau continued to forge ahead in the face of discouraging mortalities by adding minor variations to the original procedure. Amussat, the first to remove the coccyx, was followed by Verneuil in 1873, who adopted coccygectomy as a routine procedure because of the more satisfactory exposure afforded.

Kocher, in 1876, not only excised the coccyx, but removed a portion of the sacrum for the same reason. Gradually a realization of the importance of a more and more radical extirpation forced itself upon the minds of these courageous pioneers. Next on the roster of famed surgeons who devoted their skill and ingenuity to the ever widening problem of cancer of the rectum comes the name of Kraske.

In 1885 before the Fourteenth Congress of German Surgeons, Kraske presented his great contribution to the advancement of the surgical treatment of malignant disease of the rectum. The magnitude of his contribution can be judged only in the light of his time, for it combined two features of the greatest importance (1) a most radical removal of the rectum well up to the peritoneal reflection through an approach which sacrificed a portion of the sacrum, as well as the coccyx, and (2) conservation of the sphincteric mechanism.

During the next quarter of a century such men as Hochenegg, Bardenheuer, Billroth, Rehn, Rydygier, Scheiky, DePage, Hartmann, and others suggested many modifications which met with small popularity.

Perhaps the greatest single adjunct to radical removal of the rectum is the simple procedure of colostomy which far antedated even the earliest attempts at proctectomy. It has, down through the ages, paralleled the development of extensive rectal surgery, but not until well along in the nineteenth century have the two become amalgamated as basic principles in this field of endeavor. Colostomy was first recorded by Aurelianus, as having been performed by Prazagoras 400 years before Christ in an attempt to treat ileus, but the bowel was closed after having been evacuated of its contents.

Littre, in 1710, through the medium of a child who died of a congenital obstruction of the rectum, conceived the idea of a permanent colostomy. He was followed in this by Pillore and DuBoise, but not until 1793 did Duret perform a left iliac colostomy on a child with an imperforate anus. Pillore, in 1776, performed a cecostomy for rectal cancer, but it is the French surgeon, Amussat, to whom we are indebted for establishing the

principle of colostomy in the presence of cancer of the rectum. In 1839 he observed a patient dying of obstruction from rectal cancer and was thereby convinced of the desirability of colostomy which he termed a *grave* but not insupportable infirmity. Amussat developed the lumbar colostomy and during the next 15 years Baudens, Keyworth, and Phillips improved on the operation.

In 1865, Ward advocated routine lumbar colostomy in all cases of rectal cancer so that gradually the maneuver became recognized as an integral part of the operative plan of treatment. The principle of multiple stage operation was thereby established, and henceforth, development has progressed hand in hand with anesthesia and aseptic surgery to culminate in the most courageous endeavor in this field, the combined abdomino-perineal resection of the rectum.

As is often the case, progress has been the step-child of error and so it was in 1883 when Czerny performed the first single stage perineo-abdominal resection of the rectum. He found it impossible to remove a carcinoma well up in the rectum or rectosigmoid through the perineal route as intended, so he promptly opened the abdomen to complete the resection transperitoneally.

In 1887 von Volkmann published his work on the combined abdomino-perineal operation, which by the turn of the century was not only vigorously championed but considerably improved upon by Miles.

During the past 30 years the tangled web of surgical endeavor in this field has, through the ingenuity, skill, and multiplicity of ideas, culminated in the development of a number of operative procedures, the worth of which it has taken valuable time and experience to prove or disprove.

The procedure which represents the most radical attempt at extirpation of rectal cancer with block dissection of the gland bearing tissues represents the ultimate in radical surgery in this location. It is a tribute to Miles that most experienced operators of today recognize the importance of the fundamentals of his operation and after practicing various types of modification, they gradually are coming more and more to his original procedure. The modifications have been popularized largely by Pauchet in France, Labey in this country and Gabriel and Grey Turner in England.

The operation of Miles, with minor variations, has stood the test of time and in the hands of many surgeons is recognized as the operation of choice when, of course the indications for its use have been fulfilled. The efficacy of the one-stage

procedure must not, however be permitted to overshadow the distinct advantages of the graded operation for those who fail to meet the requirements of the more radical maneuver.

In the discussion of carcinoma of the rectum it must be pointed out that for three reasons it has become a problem of enlarging interest and importance during the last half century. First, there is a steady increase in the number of our population who during the past 50 years, are reaching well beyond what has been popularly referred to as the "cancer age" (40 to 70 years). For example life expectancy has been increased by 20 years during the last 8 decades, to attain the average span of 60.5 years. Second, the great wave of popular interest stimulated by educational programs and propaganda fostered by such worthy organizations as the Society for the Prevention of Cancer and others, has created a cancer consciousness which impels people to seek early medical attention. Finally and perhaps most important of all, are the vast strides which have been made in diagnostic facilities during the same period.

It has been suggested that the incidence of cancer of the rectum may be on the increase. In England and Wales statistics have shown that during the period from 1920 to 1929, the mortality from cancer of the intestine including the rectum, has increased from 6.8 to 13.6 per hundred thousand. In this country during the same period the figure has increased from 7.1 to 9.4 deaths per hundred thousand. The significance of these figures is obvious, provided this is an actual and not a relative increase dependent upon the progressive efficiency and increasing accuracy of the Bureau of Vital Statistics.

With regard to the racial distribution of cancer of the rectum, sufficient data have not been accumulated to permit of an accurate estimation. Ralford observed at the Johns Hopkins Hospital that the ratio of malignant disease of the colon in white and colored patients was about 8 to 1. In my series of 424 cases of cancer of the colon and rectum seen during the past 5 years, only 3 patients were colored—an incidence of 0.007 per cent. Of 5 patients suffering from carcinoma of the rectum and rectosigmoid only 1 of these was colored. It is generally conceded that carcinoma of the rectum occurs more frequently in men than in women. In a series of 300 cases reviewed by Rankin and Jones, the proportion of men to women was about 3 to 2 although Pfeiffer, Gabriel, and others find it to be nearer 2 to 1.

Rectal cancer is no respecter of age, although it usually occurs in patients between the fifth and

eight decades of life. In a series of 7,313 collected cases of carcinoma of the rectum, Pennington found that 37 per cent of these patients were 30 years of age or less. In a similar series of 1,452 cases reported by Rankin and Comfort, 38 per cent were found to occur in patients under 31 years of age.

In the literature a total of 25 cases of cancer of the large bowel have been reported in patients less than 18 years of age, and of these only 5 were situated in the rectum.

#### GENERAL CONSIDERATIONS

*Etiology* The etiology of cancer of the rectum as of carcinoma elsewhere in the body is still a matter of speculation. Rosser has suggested the importance of benign anorectal lesions as a precursor of malignant disease. Ewing, however, is not of this opinion. Likewise, Pennington and Jones feel that such lesions, although they are not infrequently associated with anorectal malignancy, have rarely if ever been proved the cause.

The rôle of trauma, which undoubtedly plays a part in the predisposition to malignant disease elsewhere in the body, has been viewed with suspicion because it is the rectosigmoidal vestibule, the commonest site of cancer of the large bowel, which is subjected to the effects of a change from semisolid to formed stools. Reasoning thus, however, the effect of constipation, far more commonly a feminine failing, should, if an important factor, reverse the ratio in frequency of carcinoma of the rectum between men and women, which as previously mentioned is about 3 to 1. The anal canal moreover is subjected to far greater trauma than any other part of the lower bowel, yet it is the most infrequent site of carcinoma.

The relation of polyposis to cancer of the rectum was first noted by Cripps, who in 1882 observed the familial tendency of the lesion and the frequency with which these cases developed carcinoma. Hansford concurred with Cripps in his feeling that polyps were a precursor of cancer of the colon, and later Bardenheuer and Landel presented histological evidence of the malignant transformation of these polyps. Many other observers have established this thesis although it cannot be proved that all cancers of the rectum arise from polyps.

*Pathology* The intimacy with which the gross and microscopic pathology of malignant lesions are associated with the prognosis of an individual or group of cases has through the years been more and more emphatically impressed upon the surgeon. The evolution of this relationship can be traced through generations of the closest co-opera-

tion between surgeon and pathologist and through constant effort the fundamental principles of radical surgical extirpation have been developed.

Dukes, of London, has by means of a careful examination of gross specimens with regard to depth of penetration in the bowel wall established an index of malignancy upon which he is able to gauge prognosis. Broders' prolific study of the microscopic characteristics of malignant lesions upon which he has based his work of grading the activity of neoplastic tissue has, likewise, proved an extremely reliable index by which to judge prognosis. He has observed that the more nearly the cellular elements of a new-growth approach the embryonic or undifferentiated type of tissue, the more malignant the lesion, and by the same token, the more closely these cells resemble the cellular elements of normal tissue, the lower the degree of malignancy. Having established a numerical ratio between the early and the late forms of cells, he has quartered this relationship in order to express the degree of malignancy in four grades, the first being the least, while the fourth is the most malignant.

With the exception of an occasional squamous cell carcinoma at or about the anal margin and the very rare occurrence of such a lesion arising from the rectal mucosa, the remaining carcinomas are of glandular origin. All cancers of the large intestine are said to arise from Lieberkuehn's glands. To explain the appearance of a squamous cell carcinoma developing from the mucosa, it has been maintained that regenerative cells of the glandular epithelium have the ability to produce either a secretory (glandular) or protective (squamous) epithelium.

Briefly the types of rectal carcinoma are referred to by the following descriptive terms which suggest the gross characteristics of the lesion: (1) medullary adenocarcinoma, (2) scirrhous or fibrocarcinoma, (3) mucoid or colloid adenocarcinoma, (4) papillomatous carcinoma, (5) squamous carcinoma, and, finally, (6) the melanoma, which has been variously described by some as sarcoma and by others as carcinoma. Biopsy serves to substantiate the diagnosis which can nearly always be made by palpation and visualization. However, it must be emphasized that a negative biopsy should never be taken as conclusive evidence of benignancy in the presence of a suggestive lesion.

*Anatomy* There is some controversy in regard to the relative frequency of involvement of different portions of the rectum and rectosigmoid. Because of the relative ease with which a rectosigmoidal growth may prolapse into the ampulla

of the rectum, the proctoscopist is often misled as to the actual location of the lesion. The rectosigmoidal juncture may on the mucosal surface, be marked by a clear cut line of demarcation or the transition may be so gradual that a segment 2 to 3 inches long is involved. For the sake of simplicity and accuracy the rectosigmoid has been considered to lie beneath the peritoneal reflection of the bowel and include the lower inch of the sigmoid and the upper inch of the rectum.

Edwards reports that about 80 per cent of the growths are situated within 5 to 7.5 centimeters of the anus. Grant reviewed 100 cases to find half were located in the rectum and half in the rectosigmoid. Kraske believed the rectosigmoid to be the commonest site, while in a series of 100 cases studied by Rankin and Graham, 69 were found at the rectosigmoid, 29 in the rectum proper and 2 in the anal canal. Pennington observed that of 926 cases of nonannular growth, 547 occurred on the anterior wall, 280 on the posterior wall and only 99 were situated on the lateral walls.

Of greatest importance in the problem of cancer of the rectum and rectosigmoid is the lymphatic drainage of this portion of the lower bowel, and in the last analysis it is our knowledge of this subject upon which rests the choice of operative procedures. First to recognize the full significance of the regional lymphatics with regard to surgical extirpation of the rectum and rectosigmoid for malignant disease was Miles. In a detailed study of the problem he has clearly illustrated the avenues of metastatic invasion. The rich submucosal and intramural lymphatic plexuses drain into an arborization of lymphatic channels which culminate in a trunk at the mid-portion of the inferior mesenteric artery. He observed that cancer cells may spread upward, downward, or laterally in this network and that the entire perirectal supportive structures and connective tissue as well as the rectosigmoidal mesocolon were a potential source of metastasis. Gabriel, Dukes, Bussey and others have further emphasized the importance of radical removal of all the node bearing tissues, but the painstaking and laborious work of Gilechrist and David has proved beyond a shadow of a doubt the futility of anything other than the most radical extirpation. From a study of 47 specimens of cancer of the rectum removed by the Miles technique they showed that in 63 per cent metastatic nodes were present. The specimens contained an average of 53 glands each, but the size of the growth and the duration of the symptoms had no relation to the number invaded, and they showed that by means of microscopic

examination alone could the presence of malignant tissue be determined. Palpation and gross examination were notably unreliable. They also observed, as did Miles, that with lymph blockage above the tumor retrograde metastases were found below the growth, while in lesions situated near the levator ani, metastasis along the muscle sheaths was not uncommon. It was also their contention that as squamous carcinoma of the mucocutaneous junction metastasized to glands along the superior hemorrhoidal artery as well as to the inguinal glands, radical resection of the rectum is indicated.

**Symptomatology.** The early diagnosis of cancer of the rectum and rectosigmoid depends upon the presence of signs and symptoms, the intelligence of the patient, and the alertness of the attending physician. Wherein lies the discrepancy which permits of 9 to 13 months duration of symptoms before operation, it is difficult to determine. No less tragic, however, is the incidence of hemorhoidectomy performed on patients suffering from cancer of the rectum during or after which operation the actual diagnosis is made. Jones had reported an incidence of 25 per cent in a large series of cases referred to him for operation.

Just how long after the appearance of a lesion is required for the onset of signs and symptoms is not known, but it is highly probable that from 2 to 3 months is sufficient time. In a series of 7,234 cases, Newman found the average duration of 13 1/2 months between the onset of symptoms and the diagnosis of carcinoma in this portion of the large bowel. In 300 cases Rankin and Jones found it to be 17 months, while Bradley in 167 cases reported 9.4 months.

The signs and symptoms of rectal or rectosigmoidal cancer may vary with the individual but commonest of the early manifestations are the passing of blood and change in bowel habit. The appearance of blood in or on the stool is not, however a very early symptom in the course of the disease because sufficient time must have elapsed for the lesion to have penetrated the mucosa with resulting ulceration. It may vary in quantity from scant streaking to actual hemorrhage, which has not infrequently proved to be the presenting symptom. In my series of 539 cases, bleeding was found to be present in 80.5 per cent, while in nearly one-third of the group it was the earlier manifestation of disease. Buse in a study of 1,937 cases of cancer of the rectum and sigmoid, reported bleeding in 84 per cent, Brindley 80 per cent and Roser 78 per cent.

Change in bowel habit is perhaps the commonest early symptom of rectal and rectosigmoidal

cancer, and in my series 75 per cent of those patients suffered this initial complaint. Constipation was noticed in 55 per cent, while 20 per cent suffered from diarrhea. Rosser reported that 61 per cent complained of constipation, while 22 per cent were affected with diarrhea. Constipation may be and often is a result of the obstructing tendency of the lesion, however, Miles contends that there is a functional inertia of the bowel which fails to respond readily to medication and is only rarely associated with distention. Pain, excessive weight loss, weakness, and anemia are all late manifestations of far advanced disease for which only palliative surgery can be done.

**Diagnosis** In the diagnosis of cancer of the rectum and rectosigmoid only two simple procedures are necessary. Well over 50 per cent and probably almost 80 per cent of all lesions in this portion of the bowel may be reached by the examining finger. The remainder may be visualized with little difficulty by means of the proctoscope. Available then to every practitioner is this first procedure, while the proctoscope, even in the hands of the unskilled, is of no value.

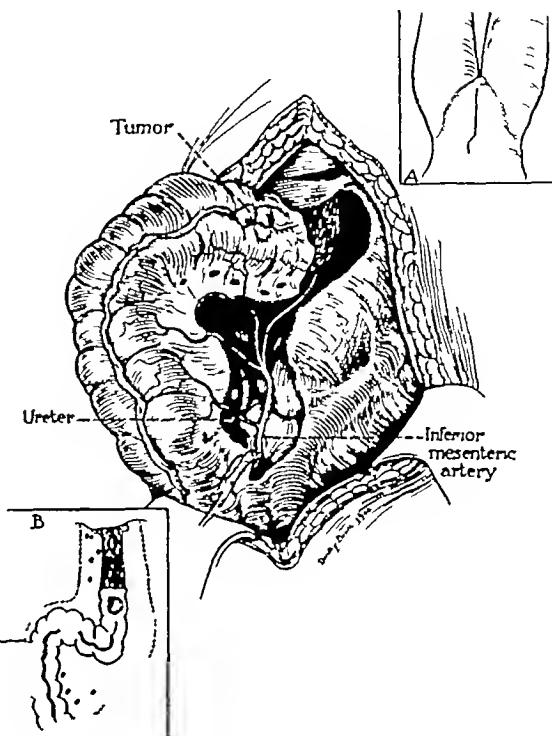


Fig 1. A, The low mid line incision. B, location of tumor, the distribution of the lymphatic supply, and the segment of bowel to be removed. The center drawing shows anatomical structures after the completed dissection of the colon. The point of ligation of the inferior mesenteric artery is indicated. The location of the tumor at the rectosigmoid juncture which is the commonest location is shown in the right lateral parietal peritoneal flap which will form a part of the new pelvic floor is demonstrated.

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### CHOICE OF OPERATION

In the treatment of cancer of the rectum and rectosigmoid the ultimate aim is to offer the most radical maneuver possible to the greatest number of patients. As has been proved by the work of Abrikosoff, Dukes, and Bussey, David and Gilchrist, only the most widespread removal of glandular tissue can be considered as a minimal procedure if a high ultimate curability figure is to be the goal of our endeavor.

In order to fulfill this dictum, therefore, such operative procedures as the combined abdomino-perineal or perineo-abdominal resection must be considered as first choice. Surgical limitations, however, exclude an appreciable percentage of cases which must, therefore, be subjected to a less formidable procedure.

The Lockhart-Mummery procedure more nearly incorporates the desirable features of the combined operation than any of the other methods.



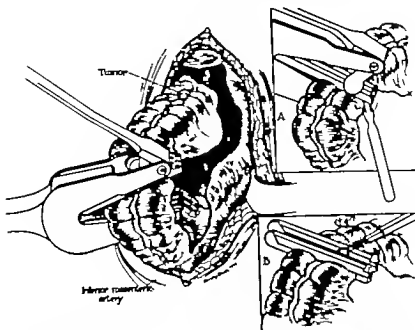


Fig. 2. The division of the bowel and the application of the Cope modification of the DeMartal clamp. A. The clamp being closed with its three clips in place. The center clip is removed and the bowel is cut with cautery between the other two, as in B.

and must therefore, be considered the procedure of choice for this second group. Neither local destruction of the cancer nor preservation of the sphincteric mechanism by segmental removal can have any effect upon the metastatic node bearing tissues, and although there may be an occasional indication for one of these procedures they can receive scant favor.

In a recent publication I have enumerated the advantages of the one-stage combined abdomino-perineal operation which are as follows (1) It conforms to the principles of radical extirpation of cancer elsewhere removing the local growth and tissues in the zones of spread (2) It permits of variations and modifications to be done in either one or two stages (3) It may be accomplished either as an abdominoperineal or as a perineo-abdominal operation (4) With increasing experience on the part of the surgeon, the operability curve may be broadened and at the same time the hospital mortality remain below 10 per cent (5) 5 year end-results from the clinics of the most experienced advocates of the radical combined procedures indicate a higher percentage of 5 year cures than for the other types of operation (6) only one laparotomy is required so that time and expense are saved for the patient (7) the blood supply to the growth may be ligated before the

pelvic dissection is undertaken (8) the procedure is applicable to all ampullary and rectosigmoidal cancers and (9) the mortality differs very slightly from that of perineal excision when operability curves are taken into consideration.

*The combined abdomino-perineal operation.* The abdomen is opened in the lower mid-line extending the incision slightly above the umbilicus and to the left in order to give adequate exposure. The abdomen is quickly explored from above downward. The surface of the right and then the left lobes of the liver are palpated for metastatic nodules and the exploring hand is passed down along the course of the aorta to determine the presence of glandular involvement. The pelvis is then examined and finally the growth itself is gently palpated to determine whether or not it is operable. In the favorable case the table is then placed in a moderate Trendelenburg position, a self-retaining retractor is fixed in place, and the small bowel is packed well into the upper abdomen.

The sigmoid is then freed from the left pelvic brim where it is frequently attached by the parietomesenteric reflection of the peritoneum. The inferior mesenteric vessels are then clamped, divided, and double ligated just distal to the left colic artery thereby leaving adequate vasculariza-

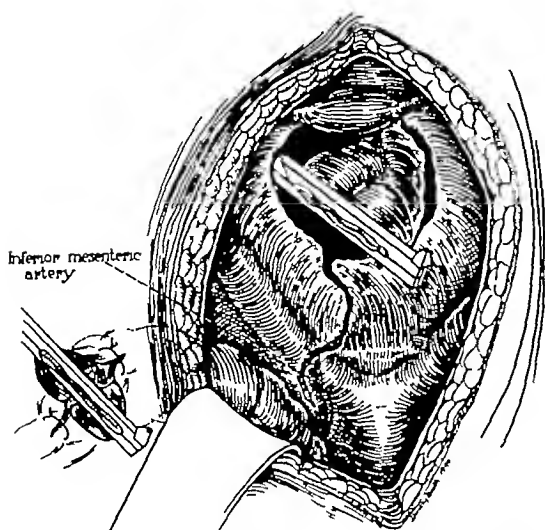


Fig 3 The completed operation and newly manufactured colostomy in the left groin. The pelvic floor has not been completely closed. The opening here exhibits the severed end of the segment to be removed which is to be dropped back retroperitoneally. The two parietal peritoneal flaps are snugly closed to form the new pelvic floor and the uterus and broad ligament are used as additional support if the patient is a female.

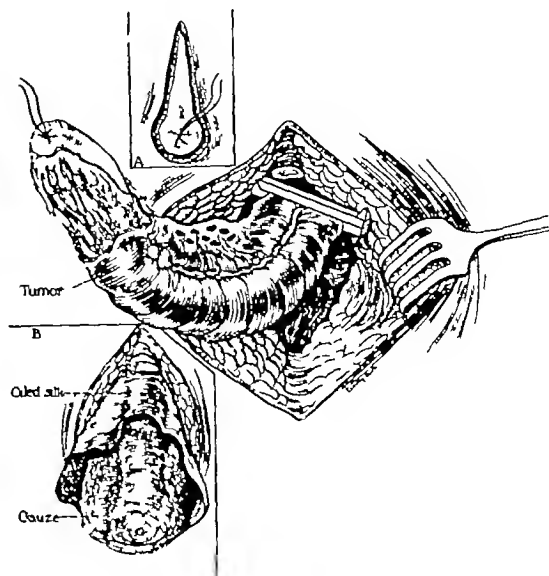


Fig 4 The posterior part of the operation. A, The type of incision. The main drawing demonstrates the completed operation with the segment to be removed in process of extraction. B, The pelvic cavity filled with a gauze pack which is encased in oil silk. A few sutures loosely close the wound over the coccyx.

tion of the upper portion of the sigmoid from which the colostomy is to be fashioned. The peritoneum covering the left side of the rectosigmoidal mesentery is then incised, and the incision is carried well down into the pelvis, but parallel to the bowel. The parietal peritoneum is then dissected free from the brim of the pelvis and downward, thus exposing the left ureter and iliac vessels. The bowel is then retracted to the left, again the peritoneum is divided well up on the mesentery and the incision extended down into the right pelvis parallel and close to the bowel. The parietal peritoneum is then freed up and the rectovesical fold in the male or the peritoneal floor of the pouch of Douglas in the female is divided and the anterior wall is dissected free. The bowel is then held forward, the hand is placed in the hollow of the sacrum, and by means of blunt dissection the upper portion of the rectum is mobilized. At this point the mesentery of the bowel is completely divided and by means of the ingenious clamp devised by DeMartel and modified by Cope, the bowel is divided with the actual cautery. Care is taken to apply the clamp at a well vascularized portion of the sigmoid, and there is left a sufficiently long segment with which to fashion the colostomy. The pelvic dissection is then carried well down behind and lateral to the rectum so

that all the gland bearing tissue is removed with it. The middle hemorrhoidal vessels are divided and ligated. The distal portion of the bowel is dropped into the pelvis and a new pelvic floor is made by the approximation of the lateral peritoneal flaps. In the female this step is somewhat easier than in the male because a portion of the broad ligament and uterus may be utilized.

A suitable site in the left groin is now chosen for the colostomy and at this point a circular area of skin 3 centimeters in diameter and including the subcutaneous fat is excised. The underlying muscles and fascia are then divided down to the peritoneum which is opened. The DeMartel clip on the upper segment of the sigmoid is then passed through this opening and the bowel is drawn gently but snugly into place. One or two sutures may be used to approximate the wound edges, but the bowel is never sutured to the abdominal wall. The clip is left in place for 36 hours.

The omentum is brought well down over the small intestine and the midline incision is closed in layers, dressings are applied, and the patient is turned on his abdomen with the hips moderately elevated.

The second half of the operation is then carried out after the snug closure of the anus with a

strong linen suture. Two concave incisions extending from the macrococcygeal junction to the mid portion of the perineum are made to include the anus and a generous portion of peri-anal skin and subcutaneous tissue. The levator ani muscles are divided well laterally and much of the peri-rectal fat is removed. The supporting ligaments of the rectum are divided and the coccyx is excised. Having once established a line of cleavage between the rectum and the prostate or in the recto-vaginal septum, dissection is carried out without difficulty. The entire portion of the lower bowel is then removed with ease. After bleeding is controlled, a sheet of oiled silk 2 feet square is placed over the posterior opening and invaginated into the depths of the pelvic cavity by means of two large gauze packs introduced with sufficient pressure to give support to the pelvic floor. The wound is partially closed with several stay sutures of silkworm gut, and a snug dressing is applied in such a manner that the buttocks are pressed firmly together.

**Postoperative treatment.** Equally meticulous attention is required during the postoperative course of these patients, and it has become my routine to give all patients in whom the bowel has been resected a transfusion of 500 cubic centimeters of citrated blood immediately after operation. Parenteral fluids to the amount of 3,500 cubic centimeters are administered daily for the first 3 days, and thereafter fluids by mouth are given in gradually increasing quantities. The patients are kept in a warm room and turned hourly until they react and thereafter every 2 hours for 24 hours. Carbon dioxide is administered routinely and adequate sedation is essential. The colostomy clip of the DeMartel clamp is removed after 36 hours, at which time the first of the two packs is removed from the posterior wound. The second is removed 24 hours later and irrigations are begun the following day. The patient is usually allowed up on the twelfth to the fourteenth day and sits baths are started immediately. The average duration of hospitalization following the combined abdomino-perineal operation is 28 days.

#### OPERABILITY, MORTALITY AND PROGNOSIS

In the evaluation of any surgical endeavor the personal equation of the operator must be taken into consideration. In order to introduce this highly important factor statistical data must include an expression of two intangibles, that is, surgical judgment and technical skill. This can be accomplished only if in a group of patients, the percentage of operable cases is co-ordinated with the mortality rate and end results, for if only a

few carefully selected individuals are subjected to operation, the mortality and end-results of this group will present a highly creditable figure; however, the remainder of the group will be afforded scant opportunity of recovery. In order to increase the availability of operative treatment the percentage of cases subjected to radical surgery must constantly be raised, while the mortality is kept as nearly fixed as possible. Only judgment and skill may widen the curves of this graph, and with their divergence end-results will take care of themselves.

It is encouraging to note the gradual increase in operability figures both in this country and in England and the Continent. Gabriel at the St. Mark's Hospital, London, has increased his operability for the decade of 1921 to 1931 by more than 20 per cent of the preceding ten years. On my service between 1915 and 1930 the figure remained close to 50 per cent, while during the 5 year period ending 1930, I have been able to operate on 75 per cent of these patients without, however, increasing the mortality to an unreasonable figure.

Table I includes patients seen in my private practice during the past 5 years. The trend of my service tends to parallel that of many of my colleagues in that more and more often we are able to use the one-stage combined abdomino-perineal operation which is unquestionably the most radical procedure available for the treatment of carcinoma of the rectum and rectosigmoid. The mortality rate, however, has not suffered through increasing the applicability of the procedure. Although fewer two-stage procedures are being performed, they are reserved for the poorer surgical risk, and I feel that the horizon of the Lockhart Mummery maneuver, colostomy and subsequent posterior resection is being extended to include more of this group than has been my wont in the past.

TABLE I.—OPERATIONS FOR CANCER OF THE RECTUM AND RECTOSIGMOID

		Mortality	
		Cases	Deaths Per cent
One-stage		7	6
Colostomy and posterior resection	4	3	75
Colostomy alone or 2nd exploration	43	0	4
Exploration alone			
Two-stage resection (Rankin)	7		
Colostomy (acute obstruction due to cancer)		3	—
		5	7
Patients	5	Resections	60
Operations	100	Resectability	75%

It is interesting to note that in this series of 112 combined abdominoperineal resections there have been 7 deaths, a mortality of 6.2 per cent, whereas, in a group of only 41 Mummery resections there have been 3 deaths, a mortality of 7.3 per cent, perhaps a little high, but with an operability figure of 75 per cent obviously many of the graver surgical risks are being afforded the opportunity of resection who would otherwise perish. It must be observed that in the evaluation of the results of this two-stage procedure the mortality following colostomy in patients who at that time were thought to be resectable, is included with the mortality of the second stage, whereas the mortality on the single-stage combined operation is in itself a true figure.

In those patients upon whom colostomy alone is performed the mortality is still higher, 14.2, and justifiably so because it is only in the last stages of disease that they present themselves. It is difficult to countenance the tendency of some who feel that colostomy in the nonresectable cases should be withheld until obstruction is actually present. Today, as in 1839, the principle of colostomy as part of the plan of treatment of cancer of the rectum established by Amussat, is still unchanged, and when it is performed earlier in the course of the illness the misery, pain, and profound toxemia incident to obstruction may be prevented. More and more the prejudice against colostomy is being overcome. Few surgeons there are who will not now admit the desirability of colostomy, and change in the attitude of the general practitioner is more encouraging.

The statistics presented by Dr D. F. Jones in 1936 are a good illustration of what may be done by the hand of a master surgeon. In a series of 672 patients 63.5 per cent were operable. In this group 165 were subjected to the one-stage combined abdominoperineal operation with a mortality of 13 per cent, and a 52.6 per cent five year cure. In 110 two stage combined operations the mortality was 27 per cent and the five year cures

reached 51.5 per cent. Mummery reported a series of 330 cases upon whom he performed the colostomy and posterior resection with a mortality of 7 per cent and a five year cure of 52 per cent. In this series there is no operability figure.

Gabriel has steadily increased his operability rate until for the year 1936 it had reached 67.8 per cent. His mortality in 100 perineal operations from 1933 to 1936 was 5 per cent, while only 37 to 40 per cent of these patients were living and well at the end of five years. In 100 patients operated on by the one-stage combined abdominoperineal operation 22 died. End results were not tabulated.

Miles in several isolated series of cases has decreased the mortality in his procedure from 25 per cent to 7.6 per cent. He reported a 73 per cent 5 year survival in a series of patients operated on from 1920 to 1925, while Abel, of London, reported a 5 year survival of 69.3 per cent following the one-stage combined abdominoperineal operation, calculating as did Mummery and Gabriel. In 151 combined abdominoperineal resections in one stage, T. E. Jones reports that he had a 10.5 per cent mortality and a 52 per cent five year survival.

This field of surgery demands a high degree of technical skill and seasoned judgment, and, if mortality figures are to be kept within reasonable limits, special training and experience are required. The establishment of a routine pre-operative preparation of the colon and physiological rehabilitation of the patient has in the past few years contributed greatly to the success of this type of surgery while meticulous postoperative care is essential. This routine, in which all those taking part in the care of these patients are carefully trained, has in my hands afforded the most gratifying results. Although the ultimate in perfection for the treatment of cancer of the rectum and rectosigmoid has by no means been reached, the vast strides which have been made during the past 25 years offer encouragement and inspiration for future advancement.

# PECTIN IN THE TREATMENT OF VARIOUS TYPES OF WOUNDS

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**E**XPERIMENTAL work undertaken to explain the excellent results obtained by the use of the apple diet (8) and, later, pectin agar preparation (3, 9, 10, 11) in diarrhea of infants, demonstrated that the pectin being used had bactericidal action under certain conditions ( ). Before subsequent work (1) showed that the bactericidal action which had been observed was due to nickel in the pectin first used, and not to pectin *per se* we had speculated on the possible therapeutic action of pectin solutions in the treatment of infected wounds. Favorable response in the first cases led to further use of the material. Clinical evidence has accumulated to show that other pectins<sup>1</sup> as well as the nickel pectin mixture have definite value in the treatment of wounds.

## METHOD

The pectin powder is used in aqueous solutions in percentages which vary according to the case to be treated. Solutions ranging from 3 per cent (on the basis of 100 grade pectin) to as high as a thick paste of 10 per cent have been used. The desired amount of pectin is weighed and mixed rapidly in cold water. For many of our cases the solution was sterilized in the autoclave for 30 minutes at 15 pounds pressure, but the addition of merthiolate makes sterilization by heat unnecessary and permits the use of a lower percentage of pectin, as heat reduces the viscosity. It was found that solutions of pectin may become contaminated with fungi, which grow in it since they are not so easily inhibited by the acidity of the solution (pH 3.4-3.8) as are most bacteria. To prevent this, aqueous merthiolate was added to make a dilution of 1:200,000. This not only prevented growth of fungi but added to the bactericidal effect of the solutions and yet was dilute enough that it was not toxic to tissue (6). Sterile gauze dressings are saturated with the pectin solution, or

the solution is applied directly to the lesions as needed. The dressings are changed as often as necessary to keep them moist. Since this is an aqueous carbohydrate solution, excessive evaporation results in a tenacious stiff dressing which is difficult to change without tearing away new tissue. However, the pectin solutions give up the moisture slowly and by using vaseline gauze, oiled silk, heavy waxed paper or paraffin over the pectin dressings with a dry dressing over that, evaporation was reduced to a minimum. When used following sequestrectomies, the pectin dressings were changed two or three times a week; those of other types of wounds, usually at least once a day. Progress of the wound was followed by bedside notes, occasional bacteriological examinations and clinical photographs.

## ANALYSIS OF STUDY

This report covers a period of three years beginning February 1936 in which 75 patients were treated by this method of therapy with very satisfactory results. These were of the following general types: 25 decubitus and trophic ulcers, 23 chronic discharging wounds, such as osteomyelitis, 19 operative wounds with drainage or second ary infection, 5 superficial wound infections and 3 traumatic wounds. Fifty-seven of these were treated with the nickel pectin solution and 18 with nickel-free pectin solution. No essential difference could be observed in the results obtained in the two groups. The addition of the merthiolate (1:200,000) also caused no apparent difference in the results. Although only 8 cases were treated with pectin solution which did not contain merthiolate, it seemed impractical to omit it for a larger series of cases, because, as has been stated, it is necessary to add a preservative to prevent the growth of fungi in the solution.

Pectin dressings in the types of wounds treated bring about a prompt visible change in the wound. The wound takes on a healthy appearance and fills in from the bottom with rapid formation of granulation tissue. This new tissue is of a smooth bright red type with a healthy glistening sheen, is firm, and shows vigorous growth. The bactericidal effect of aqueous solutions of pectin, because

<sup>1</sup>From the Departments of Pediatrics and Central Laboratories, Indiana University Medical Center. Aided by grant from Mead Johnson and Company, Evansville, Indiana. Dr. Tompkins is now associated with the University of Nebraska College of Medicine, Omaha, Nebraska.

<sup>2</sup>Merck Laboratories, Inc., New York City.  
<sup>3</sup>Kellogg furnished by General Foods Corporation, Battle Creek, Michigan.



Fig 1 a, left, Appearance of lesion on February 11, 1936, 5 years after the accident During these 5 years the wound had failed to heal sufficiently to justify attempting a skin graft b, Showing successful skin graft on April 7, 1936

of the high hydrogen-ion concentration (4, 5) and of the merthiolate and nickel, when present, appears to be only a part of the total therapeutic action. A considerable portion of the curative effect may be due to the hygroscopic property of pectin solutions which results in the decrease of edema in the granulations and leads to healthy wound healing. The granulation tissue thus formed, which is actively growing and apparently not edematous, seems to be able to rid itself of the effects of the infecting bacteria. The mechanical removal of organisms, pus, and serum, with change of dressings is probably also of some benefit. The acidity of the material does not seem to cause any irritation to tissue. Early in the course of treatment, the blood and pus in the wound decrease the acidity of the solution considerably, but at later stages of healing when very little body fluid is present, there is also no evidence of irritation. On the contrary, the application of pectin dressings to the various types of lesions decreases the discomfort according to statements of the patients, particularly in infected operative wounds. Another important feature is the absence of objectionable odors. This is especially noteworthy in cases of osteomyelitis, for the foul odors which are a very objectionable feature when some other methods of treatment are used, are not present in cases in which pectin solution is used. Their absence not only raises the morale of the patient, but also contributes to the satisfaction of the doctors, nurses, and others in the vicinity of the patient.

We do not feel that the pectin has any direct stimulating influence on epithelization, in fact,

there are some indications that pectin inhibits that stage of healing. Accordingly, when a wound is clean and has filled to the desired degree, other medications are used to keep the lesion clean while the epithelial tissue grows. Much has appeared in foreign literature concerning the hemostatic action of pectin. However, we have been unable to observe positive clinical evidence to substantiate these claims for such marked local hemostatic action. Experimental work with animals in which we have used various pectin solutions to test for general and local hemostatic action following in-



Fig 2 a, left, Lesion on October 6, 1936, at the time the pectin dressings were started b, December 12, 1936 at time of discharge



Fig. 3 a, left, Trophic ulcer on April 8, 1937. Area had become progressively larger for the past 3 years. b, 24 y. s. 1937. Comparison photograph taken after 24 days of pectin treatment.

transmucular and intravenous injections and local application gave evidence of some hemostatic action but of such a slight and transitory nature that its significance seems questionable.

Except for the osteomyelitis cases we have no comparable series to serve as controls, as accurate records of the time required for the healing of wounds and ulcers treated by other methods were not available. However controls for these types of lesions are practically impossible except in the broadest sense, for results depend on the entire treatment of the individual as well as on the local measures used, and the factor of case differences also does not permit definite comparisons. It can be stated nevertheless, that with most of our patients the results exceeded the usual expectations and that in many instances wounds that had been treated by the customary measures with no success, showed prompt response to the pectin therapy. Results were good or excellent in practically every case. One superficial burn case and the one

case of impetigo treated, failed to respond as did also a tuberculous nephrectomy wound in which sloughs continued to develop. In the osteomyelitis cases healing time following sequestrectomies was reduced about one-fourth of that required under other methods of treatment which have been used here.

Thomson reports the use of a per cent pectin solutions in the treatment of old infected burns, pressure sores, infected soft tissue wounds, osteomyelitis, and infected compound fractures, and has confirmed the results obtained here.

#### CONCLUSION

After more than 3 years use of pectin solution in the treatment of a sizable series of various types of wounds, we feel that such therapy results in a very prompt response with cleaner wounds and a rapid growth of highly vascular granulation tissue. The method seems to be of particular value

(These patients were under the supervision of Dr. George J. Gannon.)

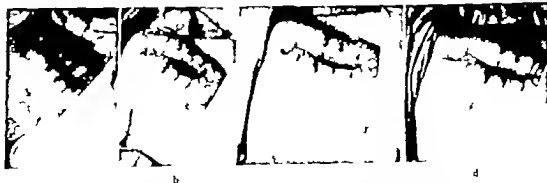


Fig. 4 a, Appearance of abdominal wound July 9, 1938, before pectin dressings were started. b, July 5, 1938, after 5 days of pectin dressing. c, August 2, 1938, after 15 days of pectin dressing. d, August 30, 1938, at time of discharge.

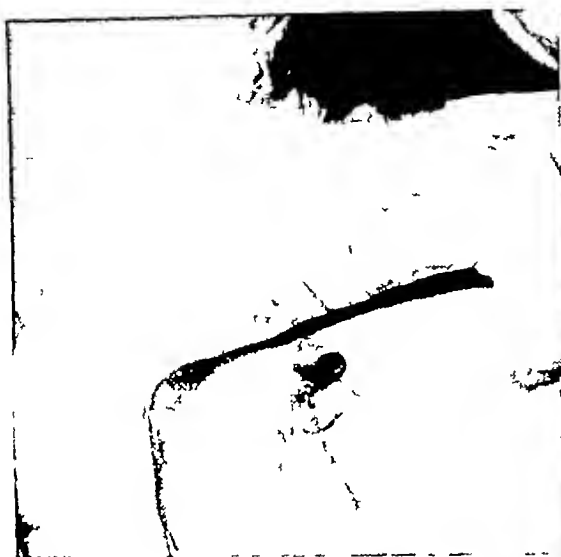


Fig 5 a, left, April 25, 1938 Pressure sore on the back of a child, which developed following the second stage



of a spinal fusion b, May 23, 1938 Photograph taken at the time the child was furloughed Back well healed

in the chronic type of lesion which often resists all other therapeutic efforts and in those in which considerable growth of granulation tissue is required. This method of treatment is being continued in our hospitals with considerable satisfaction.

#### ILLUSTRATIVE CASE REPORTS

**CASE 1** M B, a white female, aged 15 years, admitted to the hospital February 17, 1936. Her physical examination was entirely negative except for an ulcerated lesion on the right foot (Fig 1 a). The area was triangular in shape and involved a space 3 by  $1\frac{1}{2}$  inches on the medial and dorsal aspects of the foot. The foot had been injured in a train accident 5 years previous to this admission. During these intervening years she had been hospitalized at 2 different times for periods of 3 to 4 weeks. Therapy while in the hospital and at home had included chlorozone, scarlet red, merthiolate, and hot magnesium sulphate packs. Ultra violet radiation and heat cradle had also been used. The lesion had failed to show any permanent improvement and the condition of the wound had never permitted attempting a skin graft. On this admission, treatment with 1 per cent chlorozone and elevation of the foot gave no apparent results. On February 20, 1936, a culture from the lesion of the foot showed hemolytic streptococcus and Staphylococcus epidermidis. Pectin dressings were started with a 2 per cent solution of nickel pectin with 15,000 merthiolate. This was the first wound treated with pectin solution and we were unaware of the presence of nickel in the substance. The merthiolate was added to be certain the solution was sterile. However, after the first application, we decided for experimental purposes to use 2 per cent aqueous pectin solution without merthiolate.

The wound promptly assumed a clean appearance and bacterial cultures showed a rapid disappearance of the streptococcus. Healing progressed at a most satisfactory rate. On February 29, 1936, the pectin was discontinued

and chlorozone and ultraviolet were used in preparation for skin grafting. On March 13, 1936, three Thiersch skin grafts were applied. Following surgery the patient's condition was good, the grafts took well (Fig 1 b) and she was discharged on April 9, 1936, with the wound healed. A check at a year and again at 2 years after the graft, revealed that the results were excellent.

**CASE 2** J C, white male, aged 4 years, was admitted to the hospital, September 23, 1936. Physical examination and history were essentially negative except for contused and lacerated tear on the left foot which had resulted from a street accident on September 22, 1936. Lesion had been closed with a primary suture at the time of the accident. At the time of admission some necrosis was believed present but it was thought best not to do a débridement. Anti tetanus serum was given and continuous bath of  $\frac{1}{4}$  per cent chlorozone was administered. The child's temperature was irregular up to 104 degrees F. The local discharge persisted and the general condition became alarming. The sutures were removed to permit adequate drainage and several of the metatarsal bones and their joints were found to be exposed (Fig 2a). On October 6, 1936, dressings of 2 per cent nickel pectin solution without merthiolate were started. The discharge from the wound, from which Staphylococcus aureus and non hemolytic streptococcus were grown, decreased, and healthy granulation tissue proliferated at a very satisfactory rate. The temperature and general condition improved promptly and on October 22, 1936, the condition was satisfactory enough to transfer the child to the convalescent hospital where treatment was continued. On December 12, 1936, at time of discharge, the wound was healed except for a small area of granulation tissue on the dorsum of the foot (Fig 2b). The child had perfect motion of the foot, although an ankylosis of the involved joints had been expected.

**CASE 3** J E, white female, aged 10 years, was admitted to the hospital April 7, 1937. The child came in with the complaints of bilateral paralysis from the hips downward, incontinence, and ulcer on buttock. Spina bifida had been operated upon 13 hours after birth. The





Fig. 3. a, left, Trophic ulcer on April 8, 1937. Area had become progressively larger for the past 3 years. b, May 3, 1937. Comparative photograph taken after 24 days of pectin treatment.

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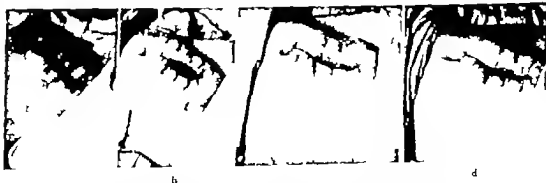


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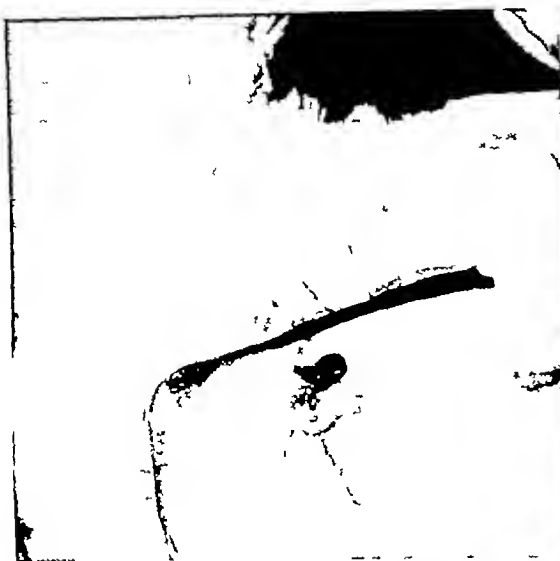


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and chlorozone and ultraviolet were used in preparation for skin grafting. On March 13, 1936, three Thiersch skin grafts were applied. Following surgery the patient's condition was good, the grafts took well (Fig 1 b) and she was discharged on April 9, 1936, with the wound healed. A check at a year and again at 2 years after the graft, revealed that the results were excellent.

**CASE 2** J C, white male, aged 4 years, was admitted to the hospital, September 23, 1936. Physical examination and history were essentially negative except for contused and lacerated tear on the left foot which had resulted from a street accident on September 22, 1936. Lesion had been closed with a primary suture at the time of the accident. At the time of admission some necrosis was believed present but it was thought best not to do a débridement. Anti-tetanus serum was given and continuous bath of  $\frac{1}{4}$  per cent chlorozone was administered. The child's temperature was irregular up to 104 degrees F. The local discharge persisted and the general condition became alarming. The stitches were removed to permit adequate drainage and several of the metatarsal bones and their joints were found to be exposed (Fig 2 a). On October 6, 1936, dressings of 2 per cent nickel pectin solution without merthiolate were started. The discharge from the wound, from which *Staphylococcus aureus* and non-hemolytic streptococcus were grown, decreased, and healthy granulation tissue proliferated at a very satisfactory rate. The temperature and general condition improved promptly and on October 22, 1936, the condition was satisfactory enough to transfer the child to the convalescent hospital where treatment was continued. On December 12, 1936, at time of discharge, the wound was healed except for a small area of granulation tissue on the dorsum of the foot (Fig 2 b). The child had perfect motion of the foot, although an ankylosis of the involved joints had been expected.

**CASE 3** J E, white female, aged 10 years, was admitted to the hospital April 7, 1937. The child came in with the complaints of bilateral paralysis from the hips downward, incontinence, and ulcer on buttock. Spina bifida had been operated upon 13 hours after birth. The



Fig. 3. a, left, Trophic ulcer on April 8, 1937. Area had become progressively larger for the past years. b, May 3, 1937. Comparative photograph taken after 24 days of pectin treatment.

intramuscular and intravenous injections and local application gave evidence of some hemostatic action but of such a slight and transitory nature that its significance seems questionable.

Except for the osteomyelitis cases we have no comparable series to serve as controls, as accurate records of the time required for the healing of wounds and ulcers treated by other methods were not available. However controls for these types of lesions are practically impossible except in the broadest sense, for results depend on the entire treatment of the individual as well as on the local measures used, and the factor of case differences also does not permit definite comparisons. It can be stated, nevertheless, that with most of our patients the results exceeded the usual expectations and that in many instances wounds that had been treated by the customary measures with no success, showed prompt response to the pectin therapy. Results were good or excellent in practically every case. One superficial burn case and the one

case of impetigo treated failed to respond as did also a tuberculous nephrectomy wound in which sinuses continued to develop. In the osteomyelitis cases healing time following sequestrectomies was reduced about one-fourth of that required under other methods of treatment which have been used here.

Thomson reports the use of 3 per cent pectin solutions in the treatment of old infected burns, pressure sores, infected soft tissue wounds, osteomyelitis, and infected compound fractures, and has confirmed the results obtained here.

#### CONCLUSION

After more than 3 years' use of pectin solution in the treatment of a sizable series of various types of wounds, we feel that such therapy results in a very prompt response with cleaner wounds and a rapid growth of highly vascular granulation tissue. The method seems to be of particular value

<sup>1</sup>These patients were under the supervision of Dr. George J. Carsons.

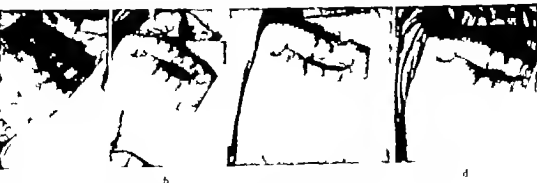


Fig. 4. a, Appearance of abdominal wound July 9, 1938, before pectin dressings are started. b, July 15, 1938, after 5 days of pectin dressings. c, August 5, 1938, after 5 days of pectin dressings. d, August 30, 1938, at time of discharge.

- 2 HAYNES, E, TOMPKINS, C A, WASHBURN, G, and WINTERS, M Bactericidal action of pectin Proc Soc. Exper Biol & Med, 1937, 36 839
- 3 HOWARD, P J, and TOMPKINS, C A Pectin agar for diarrhea in infants and the newborn, a rational, simple, and effective treatment J Am M Ass, 1940, 114 2355
- 4 PRICKETT, P S, and MILLER, N J Effect of pectin on bacterial growth Proc Soc Exper Biol & Med, 1939, 40 27
- 5 Idem In vitro effect of pectin and nickel pectin on bacterial growth J Pediat., 1939, 15 710
- 6 SALLE, A J, McOMIE, W A, and SCHECHMEISTER, I L A new method for the evaluation of germicidal substances J Bact., 1937, 34 267
- 7 THOMSON, J E M Pectin in the treatment of infected wounds Indust Med, 1938, 7 441
- 8 TOMPKINS, C A Infant diarrhea with special reference to apple therapy J Indiana State M Ass, 1935, 28 278
- 9 WASHBURN, G A pectin agar preparation in treatment of infantile diarrhea J Am Diet. Ass, 1938, 14 34
- 10 WINTERS, M, and TOMPKINS, C A A pectin agar preparation for treatment of diarrhea of infants Am J Dis Child, 1936, 52 259
- 11 WINTERS, M, TOMPKINS, C A, and CROOK, G W Pectin agar diets in the treatment of bacillary dysentery of infants and children J of Pediat., 1939, 14 788

# PRINCIPLES UNDERLYING TREATMENT OF SCOLIOSIS

By the Wedging Jacket

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**A**TTEMPT is not here made to outline the actual treatment of lateral curvature of the spine by the wedging jacket and spinal fusion. It does attempt to explain the theory of this method of treatment by assuming a simple dorsal curve and trying to explain the development and treatment of this curve. In preparing this paper the author has made free use of the material offered in the fundamental articles by Ferguson and by Butte.

It is essential in studying the efficacy of any treatment of scoliosis that accurate records of the curve be kept from the time the patient first develops the curve or from the time of her first visit to the surgeon until the time occurs when there is no further increase in the curve.

The age period from about 6 to 11 years in girls, and to about 2 years in boys is a period when increase in height is not rapid. Untreated scoliotics in this age group may show no increase in the curve, or if increase does occur it is not rapid.

Rapid increase in height occurs in girls between the ages of about 11 and 15 years, and in boys between the ages of about 12 and 16 years. During this 4 year period, the progress of the curve in a scoliotic is the most rapid (Figs. 1 and 2).

From these facts it can be said that the effect of any treatment of scoliosis in preventing progress of a structural curve cannot be proved unless the patient is accurately followed up to and through this period of rapid growth. Thus, unless the treatment of a scoliotic begins before the age of 15 and unless accurate records of the curve are kept until this rapid growth period ceases, no evaluation can be made as to the efficacy of the chosen treatment.

The accurate method of measuring the progress of a curve is by repeated comparable roentgenograms taken at stated intervals. To do this a standing anteroposterior roentgenogram is taken of the entire spine from the first sacral vertebra up. The primary curve is considered to have an apex, the most rotated vertebra which is found at the crest of the curve and an upper and lower end vertebra, the least rotated vertebra at either end of the curve. The centers of the shadows of each end vertebra and that of the apical vertebra are marked by dots. Lines are drawn from the apical

dot to each end dot. This angle is measured. The angle of the curve is the difference between the angle formed by these two lines and 180 degrees.

From the above it can be seen that accurate check is possible in these cases. If a rapid increase in a curve occurs, this demands treatment. At our present state of knowledge the only way to stop the progress of a curve is by spinal fusion of that curve. The sooner this is undertaken in a subject whose curve is increasing and who is not through the rapid growth period, the better the result will be. Exercises will not help these patients. Braces and jackets are useless (Figs. 3, 4, 5, and 6).

Operative treatment is indicated when a patient has (1) a progressive curve which will lead to poor body balance and deformity; (2) a curve which is correctable, and, if corrected, will improve either the appearance of the individual, his health, or both; (3) a curve which is causing severe pain and this can be relieved by spinal fusion.

If operation is to be undertaken, the spine should be corrected first and this degree of correction maintained by spinal fusion. This correction is obtained by the wedging jacket.

To understand the principles of correction and the area to be fused, it is necessary to assume a simple S type of curve and to follow this curve through its development, its correction, and the packing of the area to be fused. In this paper we assume the development and the treatment of a right dorsal primary curve and the development of left cervical and left lumbar compensatory (secondary) curves.

In describing the development of the following curves, the fact that weak musculature is given as the cause of the curve developing is not to be construed as the true cause. This is chosen only as a method of explaining a deforming force. The cause of this deforming force is not known. It is not known whether this deforming force is in the form of a pull or a push, but the cause or nature of this deforming force is not important here. All that is needed is to realize that there is a deforming force attempting to bring one part of the spine closer to another part. And, further if the spine is stabilized at the points where this force is acting the movement of the spine by the deforming force is made impossible (Figs. 3 and 4).

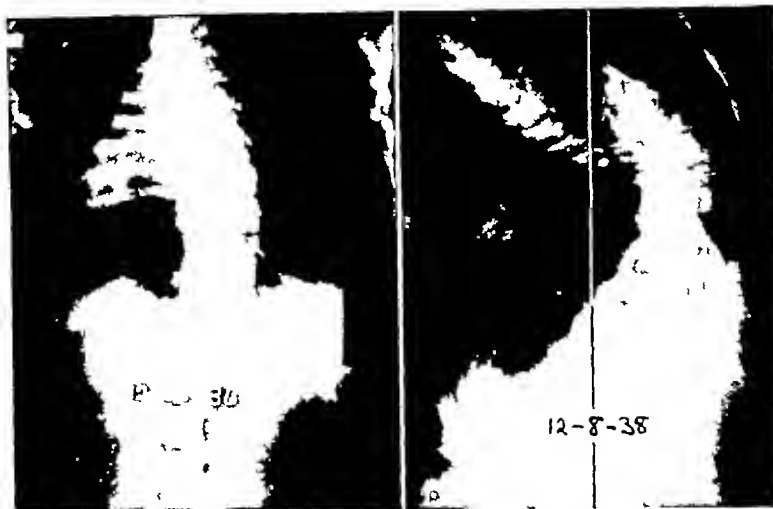


Fig 1, left At the time of this roentgenogram the patient was 11 years of age The patient had been treated with exercises, braces, and jackets since she was 7 years of age at which time the curve was first noticed Treatment up to 11 years had been considered satisfactory as the curve had not increased to any appreciable extent The years from 11 to 14 will mark the rapid growth period for this girl Primary curve from fourth dorsal to second lumbar, apex, tenth dorsal, neutral vertebra is second lumbar

Fig 2 Same girl as shown in Figure 1, 2 years later, at 13 years of age In spite of continuous treatment by exercises, braces, and jackets the curve progressed rapidly between the years of 11 and 13 Notice the great increase in the right dorsal primary curve but comparatively little increase in the compensatory lumbar curve Apparently the lumbar curve had reached its limit of compensation some time before this roentgenogram was taken Since one cannot predict which patients will show marked increase in curvature during the rapid growth period, roentgenograms every 3 months are necessary in all cases until the rapid growth period is over Right dorsal curve still from fourth dorsal to second lumbar, apex, tenth dorsal Neutral vertebra is second lumbar

The illustrations (Figs 5 and 6) show the development of a primary right dorsal curve To maintain body balance, compensatory curves have developed above and below the primary curve These secondary curves are able to keep the head centered over the pelvis until their limit of compensation is reached After this, any increase in the primary curve is not balanced by a reciprocal increase in the compensatory curves Thus, body balance is upset, and a noticeable deformity results Further, the compensatory curves are present only in response to the sense of balance If the primary curve can be decreased in the wedging jacket to the extent that the compensatory curves can again bring the head over the center of the pelvis, and the primary curve is held in this position by spinal fusion, then, clinically, the patient will appear balanced (Figs 3 and 4, 11 and 12) Or, if the primary curve is completely straightened and held straight by spinal fusion, no need for the compensatory curves exists They will straighten and the spine, too, will be straight

From the illustrations, it will be seen that a primary curve is one over which the patient has no control A compensatory curve is one over which the patient can exert control and straighten at will, provided it is not present in response to a primary curve and must from necessity be present to maintain complete or partial body balance

To distinguish a primary curve from a secondary curve, it is necessary to find the curves over which the patient has voluntary control and the curve over which the patient has no voluntary control The curves the patient can control are compensatory curves To fuse the compensatory curve with or without correction, instead of the progressing primary curve, would remove all compensatory tendencies from the spine The unfused primary curve would still increase, and the resulting deformity would be more marked than if nothing had been done Extreme in importance, then, is the picking of the true primary curve

If it were possible to place the patient in such a position that to maintain her balance, she must



Fig. 3. left. This girl is 12 years of age when this roentgenogram was taken in 1933. The curve is more marked but in general it is comparable to the curve in Figure 2. Jacket correction and spine fusion performed in 1935.

Inset roentgenogram shows final (overexposed) roentgenogram. The weighting jacket has been removed, the wire marker is over spine of the seventh dorsal vertebra.

Fig. 4. Same patient as in Figure 3, 5 years after jacket correction and spinal fusion. The patient has maintained correction through her rapid growth period and appears clinically straight. Compare with Figure 3 and note that practically all correction has been maintained and that the compensatory curves now balance the primary curve thereby achieving good balance. Contrast with Figures 3 and 4 by courtesy of the New York Orthopaedic Dispensary and Hospital.

exert control over the curve in question we could soon find out if she has control over that curve. If she has control over it, the curve is secondary. If she has no control over it, the curve is primary. This can be done. For this purpose the pelvic tilt roentgenogram is used (Fig. 7).

**Pelvic tilt roentgenogram.** These special views are taken primarily to test the muscle strength on the convex side of the lumbar curve. The patient sits on the edge of a table which is sufficiently high so as to prevent her feet resting on the floor. Her hands are in her lap giving no support to her trunk. The pelvis is now raised on the side of the

convexity of the lumbar curve (the left side of the pelvis in Figure 7) by pushing flat objects, such as boards or books, under the left buttock. A point will be reached where the patient is tilted so far toward the right that a loss of body balance is threatened, and falling to the right is imminent. If the patient is now asked to straighten up from her position, she can do so only by straightening her lumbar curve. If she can straighten her lumbar curve this curve is secondary. With the subject attempting to sit straight, an anteroposterior roentgenogram is taken of the spine from the first sacral vertebra up. Measurement of this lumbar

Fig. 5. This illustrates normal child. The musculature is represented as equal on both sides of the trunk. The child through muscle tone and sense of balance is able to hold the spine erect. If the musculature were weak or absent in the right dorsal region the muscle pull as represented by the arrows could be more marked on the left side. Muscle imbalance would be present and a dorsal curve would develop with its convexity on the right side.

Fig. 6. This figure represents absent musculature on the right side of the trunk in the dorsal area. The dorsal curve is being punched out to the right and tendency for the trunk to go off balance is present. The primary right

dorsal curve increases but through the patient's sense of balance the good musculature on both sides of the cervical and lumbar spine is stimulated to maintain balance by developing compensatory curves in the cervical and lumbar regions.

The primary dorsal curve continues to increase rapidly. The compensatory curves cannot keep pace for this increase and the trunk shifts to the right. Thus the pelvis is unable to get under the center of the trunk and appears then to stay to the left, thus making the left hip prominent. This drawing illustrates compensatory curves that are past their limit of adequate compensation. Any increase now in the primary curve will result in complete

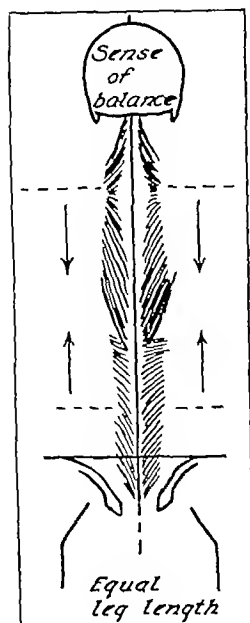


Fig 5

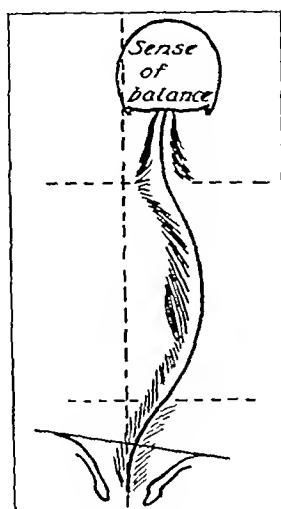


Fig 6

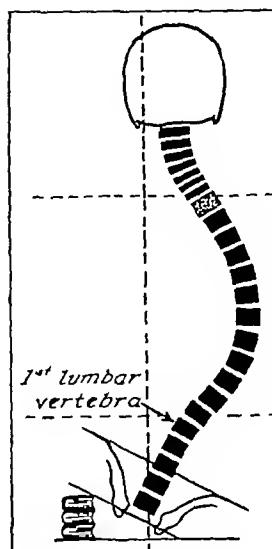


Fig 7

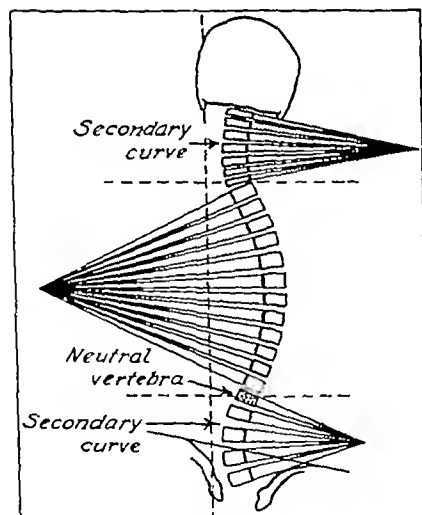


Fig 8

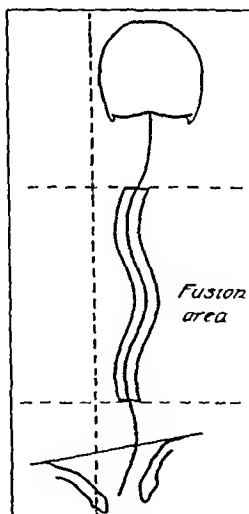


Fig 9

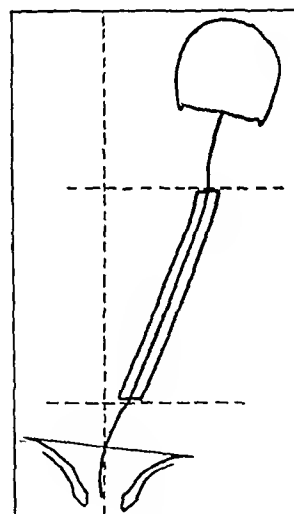


Fig 10

uncompensated deformity (Compare with Figs 1, 2, 3, and 4)

Fig 7 This left pelvic tilt plate represents the same curve as is shown in Figure 6. The primary right dorsal curve is shown as first dorsal to twelfth dorsal. The neutral vertebrae are the first dorsal and first lumbar. The tilting of the left pelvis has caused the lumbar spine to straighten completely. In this position the lumbar spine is the true axis of the trunk. All vertebrae below the first lumbar are straight and in line. The second lumbar vertebra in this case would be an ideal base for the solid column to rest

upon. The ideal result in this case would then be obtained by wedging the dorsal spine completely straight if this can be done without overcorrecting the ends of the primary dorsal curve.

Fig 8 Method of picking the extent of the different spinal curves. Note how lines change direction on each side of the neutral vertebra. Same curve as shown in Figures 6 and 7.

Fig 9 End result of overcorrecting the ends of the primary right dorsal curve and then fusing them in an overcorrected position.

Fig 10 End result of wedging the primary right dorsal curve straight and fusing the dorsal curve in this position when it has been shown by pelvic tilt that the lumbar spine is unable to straighten completely.





Fig. 1. Appearance of patient on admission to New York Orthopaedic Dispensary. Roentgenogram shows pseudoarthrosis. Fusion mass of inadequate length. Patient placed in edging jacket and corrected through pseudoarthrosis. These repaired and fusion area extended to include third lumbar vertebra.



Fig. 2. The same patient 5 years after repair of pseudoarthrosis and extension of the fusion area to include the third lumbar vertebra. Notice that moderate primary right dorsal curve still exists but fair balance has been achieved. With this as standard the result obtained in the case shown in Figure 4 may be better visualized. (Courtesy of the New York Orthopaedic Dispensary and Hospital.)

curve as compared with the lumbar curve in the standing few will give the answer to the problem (Figs. 7 and 8).

If on the other hand, the right side of the pelvis is tilted in a similar manner the left lumbar curve will increase. The right dorsal curve would then decrease in degree of curvature if it were secondary. Because of the immobilizing effect of the thoracic cage, a secondary curve in the thoracic region will not decrease as much as a secondary curve in the lumbar region when responding to the productive force.

If the right dorsal curve is primary it will not decrease in degree of curvature with the right pelvis raised any more than a primary left lumbar curve will decrease in degree of curvature when the left side of the pelvis is elevated.

In conclusion then

1. If the left lumbar curve is a compensatory curve it will decrease in the degree of curvature when the left side of the pelvis is raised (Fig. 7).
2. If the left lumbar curve is primary it will not decrease in the degree of curvature when the left side of the pelvis is raised.

3 If the right dorsal curve is a compensatory curve, it will decrease in degree of curvature when the right side of the pelvis is raised, but not to the degree that a compensatory lumbar curve of similar degree would decrease

4 If the right dorsal curve is primary, it will not decrease in the degree of curvature when the right side of the pelvis is raised. The patient is powerless to straighten a primary curve, whether it be dorsal or lumbar

#### CLINICAL FINDINGS THAT AID IN DETERMINING THE PRIMARY CURVE IN THE SIMPLE "S" TYPE

1 The prominent hip is usually on the side opposite the convexity of the primary curve. If the hip findings and the pelvic tilt findings do not coincide with each other, detailed study of the patient to determine why not is essential

2 The primary curve is usually the middle one of the three curves

3 The primary curve is usually the greatest in degree of curvature because (a) the primary curve develops faster than the compensatory curves and (b) as far as is known, the compensatory curves never overcompensate for a primary curve

If these statements are accepted, the following information has been gained

1 The primary curve in the illustrations is considered to be the dorsal curve as it is taken to act as in Figures 6 and 7

2 This primary dorsal curve has a deforming force working on it which is attempting to approximate one end of this curve to the other end. This must be stopped. To stop the effect of this deforming force on the primary curve, the whole area on which this deforming force is working must be fused

3 To find this whole area, there must be a method of determining where the primary curve starts and where the primary curve ends—a method by which one can tell the extremes of the area on which the deforming force is working, that is, the upper and lower end vertebræ of the primary curve

*Choosing the extent of the primary curve* The primary curve has an apex, the most rotated vertebra in the crest of the curve. The primary curve has also an upper and lower end vertebra, and these end vertebræ mark the extent of the primary curve (Figs 1 and 2). In looking at the standing roentgenogram of the spine (Figs 1 and 2) the apical vertebra of the primary dorsal curve is located. As the eye travels from this apical vertebra to either end of the primary curve, it will be seen that the vertebræ of the primary curve become gradually less rotated and finally a ver-

tebra is reached at each end of the curve which is not rotated. Beyond these unrotated vertebræ, the compensatory curves are beginning, and the vertebræ in the compensatory curves are rotated in the opposite direction than in the primary curve

Further, the vertebræ in the primary right dorsal curve seem to be tilted so that the interspaces between the vertebræ appear more open on the right than on the left side of the vertebræ. If this tilt is followed from the middle both ways, it will be seen that this tilt becomes less marked as the ends of the primary curve are reached. At each end of the primary curve, there will be a vertebra in which the interspace is practically uniform in height between it and the vertebra next to it on the primary curve side. This vertebra is termed a neutral vertebra. If the eye follows along the spine away from this neutral vertebra in the direction of the compensatory curve, the vertebræ in the compensatory curve will be seen to tilt. But now the interspaces will be more open on the left instead of the right side. This neutral vertebra marks the end of the primary curve and the beginning of the compensatory curve (Figs 1, 2, and 8). In this way the extent of the primary curve is found. The full extent of the primary curve is designated as the minimal fusion area

#### AREA TO BE FUSED

Considering the area to be fused

1 If, in an accurate pelvic tilt roentgenogram, it is seen that the compensatory lumbar curve has the power to return to the erect, this means that the primary curve can be straightened completely if possible. If the primary curve is wedged straight and is fused in this position, and the patient is released from all support after fusion is complete, the compensatory curves are able to bring the head over the center of the pelvis, and good to perfect balance is achieved. Thus, if the compensatory lumbar curve straightens completely on the pelvic tilt, one can give the primary curve all it will take in the way of straightening. In straightening a primary curve, it is important that it be brought only to the erect. It is very important that whether the apex of the primary curve straightens out completely or not, that the ends of the primary curve be not overcorrected. If the ends of the primary curve are overcorrected, and the curve fused in this position, the compensatory curves will have to be in the other direction, that is, reverse themselves, to compensate for this overcorrection. Body balance is again lost by this, but now in the opposite direction than before operation (Fig 9)

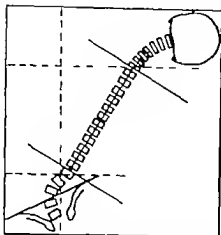


Fig. 3. Patient (Fig. 7) in wedging jacket after the dorsal spine has been completely straightened. Note that the lumbar spine is bent markedly in the direction of compensation. Also that the surfaces of the seventh cervical and the first lumbar vertebrae are practically parallel to each other and that lines joining the centers of these two vertebrae meet their transverse surfaces at right angle. This illustrates the ideal. This figure represents final (marker) roentgenogram, since correction has been continued to the point where the best possible degree of body balance will be obtained.

2. To achieve good body balance, it is essential that the primary curve and the compensatory curves work together. If, on pelvic tilt examination, the compensatory lumbar curve does not straighten completely this will mean that the primary dorsal curve should not be straightened completely. The reason some compensatory curves have not the power to return to the erect is that they have been present for a long time and tend to become fixed, or the primary curve covers such a large extent of the spine that there is not enough of the compensatory curve to allow return to the erect. Control, however, is still active to a degree.

If the primary right dorsal curve were straightened out completely and fused in this position in the face of a compensatory lumbar curve that had been shown to be unable to straighten completely the patient would be unable to bring the trunk completely back to the erect and, consequently would be left with a list toward the right (Fig. 10).

A mean, therefore, must be established in which the compensatory curves balance the primary curve. Thus, the whole will be a straight line between the center of the head and the center of the pelvis, regardless of the spinal curves in between (Figs. 1 to 4, 1 and 13).

3. In each vertebral joint there is so much motion. Decompenetration occurs when the compensa-

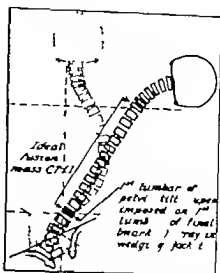


Fig. 4. Dotted figure represents pelvic tilt plate (Fig. 7). Note that the dotted lumbar vertebrae (pelvic tilt plate) are in direct line with the solid final dorsal vertebrae of the marker-ray plate (Fig. 3). The compensatory curve (composed of the lumbar vertebrae of the pelvic tilt and the dorsal vertebrae of the final roentgenogram) is straight.

tory curves reach the degree of curvature that utilizes the movement inherent in the vertebral joints making up the compensatory curves. The compensatory curves then can go no farther in the way of compensation. Any increase in the primary curve beyond the limit of secondary curve compensation will lead to an uncompensated deformity which is permanent unless treated (Fig. 6).

If, then, a compensatory curve is shown by pelvic tilt examination to be able to straighten completely, what mistake at operation could be made to prevent the complete straightening of this compensatory curve? The mistake would be to fuse into the compensatory curve to such an extent that in the vertebral joints of the compensatory curve spared at fusion there would not be enough motion left to enable the spine to return to the erect. In other words, the fusion area would be too long. This might occur at either end of the primary curve.

4. If the area fused at operation is too short all of the primary curve will not be included in the fusion mass. When all support is removed, the compensatory curves which are capable of balancing the patient are forced to compensate for the area of the primary curve not in the fusion mass. The patient will develop the same deformity as before operation, only to a lesser degree. If the primary curve increases in the unfused portion of the spine, this decompenetration may be-



port there would then be a list of the trunk to the right. Before operation the left hip was prominent (Fig. 6) but after operation the right hip would be prominent. The fusion area would be too long.

The question now arises: How can one visualize the end-result, and thus select the ideal fusion area in cases in which complete straightening of the primary curve does not occur? This is done by superimposing the final (marker) roentgenogram in such a way that the end vertebra of the proposed column, as shown in the marker roentgenogram, rests on its proposed base as shown in the pelvic tilt plate (Fig. 14). If faulty selection has occurred, superimposition will show the error (Fig. 15). Correctly done this procedure will obviate the mistake of fusing too long or too short an area.

The final fusion area can then be visualized only after the wedging is completed. It is, in effect, matching the degree of straightening of the compensatory lumbar curve, as shown by the pelvic tilt roentgenogram, with the degree of straightening of the primary curve as obtained in the wedging jacket.

Obviously after alignment is obtained, any loss or increase of correction would alter the extent of the fusion area and the degree of balance. This is why the jacket is fenestrated and all operations are carried out while the patient is in the wedging jacket. To avoid loss of correction after operation, the patient is kept in the wedging jacket for a period of at least 3 months before the semi-rigid jacket is applied, and the patient allowed up.

**Pseudo-arthritis.** In one group of surgeons experienced in this operation pseudo-arthritis occurs in about 10 per cent of the cases operated upon. The failure of one vertebral joint to fuse in the primary curve is enough to allow loss of correction sufficient to cause a loss of body balance. When a pseudo-arthritis occurs, the curve increases, and the patient retrogresses toward the decompensation present previous to operation. If a pseudo-arthritis is present and is found only after body balance is lost, jacket correction through the site of pseudo-arthritis is done, and then the defect is repaired (Figs. 1 and 2).

The presence of pseudo-arthritis should be suspected (1) when there is pain and tenderness in the fused area of the spine (2) when there is quite pronounced loss of sitting height (3) when a definite line of defect in the fusion mass is shown by roentgenogram (4) when the roentgenogram

shows an abnormal tilt of one or more of the vertebrae in the fusion mass as compared to the position of these vertebrae as shown in the roentgenogram taken previously of fusion mass (5) when there is a steady marked increase of curvature in the primary curve, either while patient is in the body jackets or after release from all support.

Normally there is a settling of the solid fusion mass the first year after operation which allows some increase in the primary curve. The amount of this increase is not definite. In general, a loss of 15 degrees in moderate curves is to be expected. The more marked the curve, the greater the degree of settling. This settling must be allowed for when estimating the extent of the area to be fused.

If a pseudo-arthritis is suspected, the spine should be explored before loss of correction is marked, and the defect repaired.

#### CONCLUSIONS

1. The majority of scolioses, with or without conservative treatment, do not develop a marked degree of curvature.

2. Since one cannot predict which child will develop a marked degree of curvature, all patients should have comparable roentgenograms taken of the spine every 3 months until the danger of further increase in curvature is past.

3. The great increase in the primary curve occurs during the rapid growth period.

4. If a curve is shown to be increasing, the sooner the patient is corrected and fused, the better the result will be. One should not wait until the rapid growth period is over to begin operative treatment, but should begin the treatment as soon as it is indicated. In this way the amount of correction to be gained is less, the spine is more flexible, the distortion of the thoracic cage is not as marked and the result is far better.

5. At the present state of knowledge of this condition, early correction of the progressing curve by the wedging jacket and the maintenance of this correction by spinal fusion seems to be the method of choice. It is the only method that will prevent the marked deformity that occurs in a certain percentage of children afflicted by scoliosis.

#### REFERENCES

- BUTLER, F. L. Scoliosis treated by the wedging jacket. *J. Bone & Joint Surg.* 1935, 30, 171.  
FERGUSON, A. B. The study and treatment of scoliosis. *South M. J.* 1930, 3, 16.

# THE TREATMENT OF FISTULA AND OBSTRUCTION OF THE SMALL INTESTINE BY COMPLETE EXCLUSION

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THE operation of complete exclusion offers certain advantages in the treatment of fistula and of obstruction of the small intestine. Although not new, the operation is generally unfamiliar. Its advantages for fistula are first, the restoration of the continuity of the intestinal tract by an anastomosis around the fistulous segment of intestine. Second, the complete exclusion of the fistulous segment, which may be excised then or later as desired. Third, the performance of the operation in a clean field well away from the fistula. Fourth, the fact that the operation is well tolerated even by debilitated individuals. The operation recently was performed on 3 patients with fistula of the ileum, and proved a life-saving measure after other standard procedures had failed.

The exclusion operation is of further value in acute obstruction with gangrene of the small intestine, because it effectively controls fistula following exteriorization of nonviable intestine. This is illustrated by the treatment of the first and second patients of this series. Both patients had gangrene of the ileum, both were debilitated, and neither would have tolerated resection of the gangrenous ileum with anastomosis at the original operation for acute obstruction. Exteriorization was performed, yet the fistula which resulted resisted all attempts at closure by stages 3 and 4 of the Mikulicz operation, and persisted despite attempts at closure by mechanical methods. At a time when the patients were failing rapidly, the exclusion operation was executed. Both patients made a rapid recovery.

The exclusion operation is applicable to any type of fistula of the small intestine. It was successfully performed on the third patient of this series for fistula due to terminal ileitis. Indeed, intestinal exclusion was originally devised to treat adhesions or tumors, but its use for fistula is relatively recent.

## LITERATURE

Trendelenburg, in 1885, and von Hacker, in 1888, first described the principle of intestinal ex-

clusion. Salzer, in 1891, used it for lesions of the cecum, and a modification of his procedure is familiar today in the form of end-to-side ileocolostomy with partial exclusion of the cecum. The Devine operation for inoperable carcinoma of the stomach represents another type of partial intestinal exclusion.

To control fistulas of the small intestine, Cokkinis and Ginzburg employed the operation of complete exclusion. Cokkinis, in 1936, reported a patient with strangulated femoral hernia and gangrene of the ileum. He resected the ileum by a Mikulicz exteriorization procedure. To close the resulting fistula he performed the complete exclusion operation and after 11 months excised the blind fistulous segment of intestine. Ginzburg, in 1940, reported the use of the complete exclusion operation in 6 patients with fecal fistulas due to terminal ileitis.

## OPERATIVE PRINCIPLES AND TECHNIQUE

The purpose of the complete exclusion operation is to restore the continuity of the intestine, and to remove completely the intestinal current from the fistulous segment of intestine. The operation is therefore called complete exclusion, and is sometimes also referred to as bilateral exclusion. It must be distinguished carefully from the operation of partial or unilateral exclusion, in which the fecal current is only partially diverted from the fistulous segment. This distinction is important, and failure to appreciate it has, at times, led to failure to close a fistula. Hereafter, when the term "exclusion" or "exclusion operation" is used alone, it refers only to complete exclusion, and not to partial exclusion.

The steps in the operation of complete exclusion are as follows. The incision is made well away from the fistula, through fresh skin, and ordinarily through the left rectus muscle. The peritoneum is thereby incised at a distance from those adhesions or abscesses which may surround the fistula.

Catheters are now inserted by an assistant through the fistula, one into the proximal and one into the distal loop of intestine. The surgeon next identifies both these loops within the abdomen, and severs each between clamps (Fig. 1). He in-

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verts the two ends which lead to the fistulous segment of intestine and replaces them within the abdomen. He anastomoses the two remaining ends, the side-to-side technique being here employed. The abdomen is closed without drainage.

Following operation the fecal current again flows entirely within normal channels, and none reaches the fistulous segment. The latter becomes a blind pocket of intestine without digestive function, and secretes small quantities of non-irritating chyme. It functions as an effective plug against herniation, being anchored posteriorly by the mesentery and anteriorly by the fistulous tract itself. In this form it may be left indefinitely or removed at a later operation.

### CASE REPORTS

**CASE 1.** Mrs. A. A. Hoesen, 46, aged 7 years, was seen by courtesy of Dr. Walter Fluebel. She was admitted to St. Luke Hospital (No. 2448) on March 6, 1930, with acute intestinal obstruction of hours' duration. The obstruction was due to strangulation of postoperative ventral hernia. Laparotomy for acute appendicitis had been performed in 1929 through right rectus incision, and a hernia resulted which had periodically become strangulated during the years 1929 to 1930, but had not previously been irreducible. Exploration revealed about one-third of meter of high ileum to be gangrenous. Due to the poor condition of the patient an obstructive resection was done. The gangrenous intestine was exteriorized and resected between clamps, and the two loops are left side by side on the abdomen. The wound was closed to the loops, but the hernia was not repaired. The clamps are removed the next day and the spur is crushed on the third day. The wound healed as far as the stomach. There

was severe skin excoriation and large portion of the intestinal secretion was lost through the fistula. Mechanical measures, such as bottles and tubes, failed to return the fecal current to the normal channel. On the eighth postoperative day an attempt was made to close the fistula by the fourth stage of the Mikulicz procedure under local anesthesia. The two loops of intestine were dissected away from the skin and subcutaneous tissue down to the peritoneum, and were anastomosed. The skin was closed over them. However, the fistula recurred days later and the patient failed, this time more rapidly than before. On March 5, 1931, the exclusion operation was performed (Fig. 1, K.) under ether anesthesia as illustrated in Figure 1. Note that the anastomosis was near the site of Meckel's diverticulum. There was immediate and rapid improvement. Aside from an infection of the left parotid gland, there were no complications and the patient was discharged May 1, 1931. She resumed her duties thereafter and has been performing household duties during the subsequent 4 months. The blind fistula (Fig. 1) discharges mucus which does not irritate the skin and which necessitates light dressings three or four times daily. A surgical support is worn. The hernia is effectively plugged by the blind loops and there has been no further strangulation. The patient refuses resection of the blind loops.

The fistula which developed in the mid-ileum of a woman of 71 after obstructive resection of gangrenous ileum strangulated in postoperative ventral hernia could not be closed by stages 3 and

4 of the Mikulicz procedure or by mechanical measures. The operation of complete exclusion was successful. The patient has worked for over a year since. The hernia is plugged by the blind loops of the excluded intestine (Figs. 2 and 3).

**CASE 2.** Dr. A. M. Rabbl, aged 7 years, was seen by courtesy of Dr. Alfred Fleckman. The patient was admitted to the Jewish Hospital (No. 10027) on February 7, 1930, with an acute intestinal obstruction of 3 hours' duration. Exploration revealed meters of gangrenous mid-ileum which had herniated through defect in the mesentery of another loop and in so doing had strangulated its own mesentery. An obstructive resection was done immediately with exteriorization of the diseased intestine. The proximal and distal loops being brought out together and clamps left applied. Anastomosis was not done because of the patient's precarious condition. On the third postoperative day the clamps are removed from both loops and double-barrel ileostomy resulted. The wound healed by primary union. On the seventh postoperative day the spur was crushed. Large amounts of intestinal juices were lost through the fistula and the patient rapidly became worse. The crushing of the spur did not help to return the fecal stream to normal channels. Catheters and curved glass tubes also proved unsuccessful in obtaining the drainage from the proximal into the distal loop. On the twentieth postoperative day under spinal anesthesia the fistula was closed by mobilization and end-to-end anastomosis. The anastomosis was not replaced within the abdomen but was left extraperitoneal beneath the skin. The fistula recurred and the patient's condition became critical. It was decided to do the exclusion operation. For 3 days prior to this, Miller Abbott tube was inserted into the distal loop for feeding purposes, and to prevent regurgitation from this loop. This measure helped no little in preparing the patient. On March 30, 1930, under local and cyclopropane anesthesia, the exclusion operation (Fig. 2) was performed (I C M.). The patient made an excellent recovery, and the wound healed. The patient was discharged April 1, 1931, and the blind loops, measuring 5 and 30 centimeters respectively (Fig. 3) are resected under general anesthesia. The defect in the abdominal wall was repaired as for postoperative hernia. Recovery was excellent, and the patient has since resumed his duties.

A fistula developed high in the ileum of a man of 71 after obstructive resection of a gangrenous segment strangulated in a defect in the mesentery. The operation of complete exclusion was successful after other measures had failed. Ten weeks later the blind loops were successfully resected.

**CASE 3.** M. J. H. an eccentricist, aged 45 years, developed regional enteritis of the jejunum about 1917. Medical treatment proved unsatisfactory. Surgery in 1925 consisted in entero-enterostomy about the diseased jejunum, and in 1927 the diseased jejunum was resected. Following temporary improvement, enteritis flared up in the terminal ileum. Surgery in 1929 consisted in two-stage resection of the terminal ileum and of the right half of the colon. A fistula appeared for the first time subsequent to the second stage, on July 7, 1929. The fistula originated from the inserted end of the ileum, and ran along posterior stab wound to terminate in the right flank. The fistula proved despite local measures and laparotomy for cure was performed on December 30, 1929. Through right subcostal incision, the tract was excised after it was traced to its origin in

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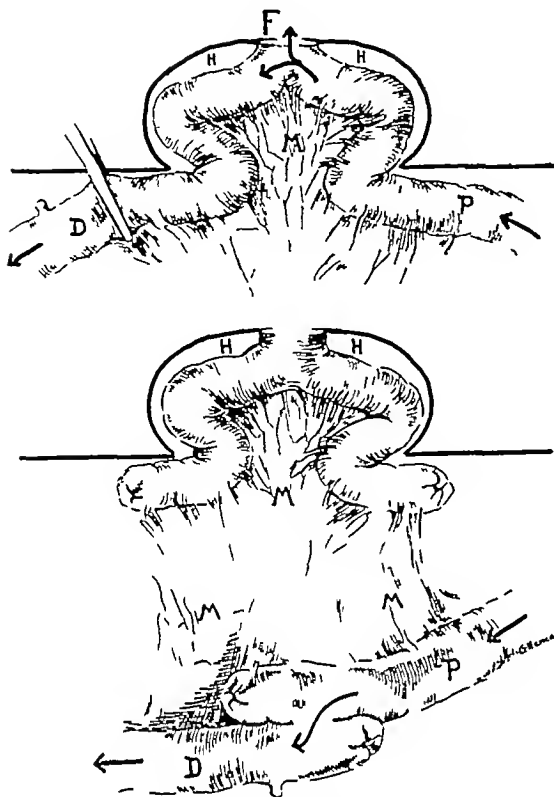


Fig 1 The complete exclusion operation, Case 1. A, above, uncontrollable fistula following exteriorization of gangrenous ileum. B, below, operation ended, fistula completely excluded. F, fistula, H, hernia, M, mesentery, P, proximal loop, D, distal loop. A Meckel's diverticulum is indicated.

the terminal ileum beyond the anastomosis. The ileum and colon in this region were dissected free in an effort to find intestine suitable for re anastomosis, but the ileitis, scar tissue, and burrowing abscesses were too extensive, and the operation was concluded by marsupialization of the open end of ileum. A huge fistula of the ileum at its junction with the transverse colon resulted (Fig 5). The fistula was successfully plugged with sponge rubber for 2 months, but the ileum then became too irritable any longer to tolerate the plug. Almost the entire fecal stream was lost and the patient's condition became bad. In view of its success in Case 1, the exclusion operation was again chosen, and was performed (E.L.K.) on April 1, 1940 (Fig 5). Convalescence was rapid, and the patient was discharged on the nineteenth postoperative day. He gained weight and has worked steadily since May 20, 1940.

A fistula developed in the high ileum of a man of 45 as a result of operations for regional ileitis. Failure followed attempts to close the fistula by operation, and the situation became critical. The operation of complete exclusion proved successful. The patient resumed work 1 month later.



Fig 2 View of first patient to show hernia plugged by the blind fistula following its complete exclusion by operation. This figure corresponds to Figure 1B. The left rectus scar results from the complete exclusion operation.

#### ADVANTAGES OF COMPLETE EXCLUSION

The operation of complete exclusion proved successful in treating three debilitated individuals with persistent fistula high in the ileum. By this operation, and after failure of other methods, the continuity of the intestinal tract was restored at a critical time.

The complete exclusion operation offers a means of overcoming certain difficulties sometimes insurmountable by the three standard surgical procedures for treating fistula. The salient points will be discussed as they relate to the three operations, namely (1) exteriorization of the Mikulicz type, (2) the one-stage operation of excision of the fistulous tract, resection of the fistulous segment of intestine, and immediate anastomosis, (3) the operation of partial exclusion, including (a) side-to-side and (b) end-to-side anastomosis around the fistula.

*1 Exteriorization of the Mikulicz type.* Gangrenous small intestine causing acute obstruction is frequently exteriorized because this operation is less dangerous than primary resection with anastomosis. The plan then is to close the resulting fistula by crushing the spur and later by anastomosis. Fistulas of the small intestine, however, can rarely be closed by such simple steps, and many deaths occur due to fistulas persisting despite these maneuvers. It was the plan in Cases 1 and 2 of this series to close the fistulas by these stages of the Mikulicz operation, but the fistulas would not remain closed. Neither patient



verts the two ends which lead to the fistulous segment of intestine, and replaces them within the abdomen. He anastomoses the two remaining ends, the side-to-side technique being here employed. The abdomen is closed without drainage.

Following operation, the fecal current again flows entirely within normal channels, and none reaches the fistulous segment. The latter becomes a blind pocket of intestine without digestive function, and secretes small quantities of non-irritating chyme. It functions as an effective plug against herniation being anchored posteriorly by the mesentery and anteriorly by the fistulous tract itself. In this form it may be left indefinitely or removed at a later operation.

#### CASE REPORTS

**CASE 1.** Mrs. A. A. Rosencoff, aged 7 years, as seen by courtesy of Dr. Walter Fischel. She was admitted to St. Luke's Hospital (No. 2448) on March 4, 1930, (th acute intestinal obstruction of hours' duration). The obstruction was due to strangulation of postoperative ventral hernia. Laparotomy for acute appendicitis had been performed in 1929 through right rectus incision, and

hernia recurred which had periodically become strangulated during the years 1929-1930, but had never previously been irreducible. Exploration revealed about one-third of meter of high ileum to be gangrenous. Due to the poor condition of the patient an obstructive resection was done. The gangrenous intestine was exteriorized and resected between clamps, and the two loops are left side by side on the abdomen. The wound was closed to the loops, but the hernia was not repaired. The clamps were removed the next day and the spur was crushed on the third day. The wound healed as far as the stoma. There

as severe skin excoriation and large portion of the intestinal secretion was lost through the fistula. Mechanical measures, such as buttons and tubes, failed to return the fecal current to the normal channel. On the eighth post-operative day an attempt was made to close the fistula by the fourth stage of the Mikulicz procedure under local anesthesia. The two loops of intestine are dissected away from the skin and subcutaneous tissue down to the peritoneum, and are anastomosed. The skin is closed over them. However, the fistula recurred, days later and the patient failed, this time more rapidly than before. On March 8, 1930, the exclusion operation was performed (E. L. K.) under ether anesthesia as illustrated in Figure 1.

Note that the anastomosis was near the site of Meckel's diverticulum. There was immediate and rapid improvement. Aside from an infection of the left parotid gland, there were no complications and the patient was discharged May 1, 1930. She resumed work shortly thereafter and has been performing household duties during the subsequent 14 months. The blind fistula (Fig. 2) discharges mucus which does not irritate the skin and which necessitates light dressings three or four times daily. A surgical support is worn. The hernia is effectively plugged by the blind loops and there has been no further strangulation. The patient refuses resection of the blind loops.

The fistula which developed in the mid-ileum of a woman of 71 after obstructive resection of gangrenous ileum strangulated in a postoperative ventral hernia could not be closed by stages 3 and

4 of the Mikulicz procedure or by mechanical measures. The operation of complete exclusion was successful. The patient has worked for over a year since. The hernia is plugged by the blind loops of the excluded intestine (Figs. 1 and 3).

**CASE 2.** Dr. A. M. Rabbil, aged 7 years, as seen by courtesy of Dr. Alfred Fielesman. The patient was admitted to the Jewish Hospital (No. 100307) on February 7, 1930, with an acute intestinal obstruction of 8 hours' duration. Exploration revealed meters of gangrenous mid-ileum which had herniated through defect in the mesentery of another loop and in so doing had strangulated its own mesentery. An obstructive resection was done immediately. Its exteriorization of the diseased intestine the proximal and distal loops being brought out together and clamps left applied. Anastomosis was not done because of the patient's precarious condition. On the third postoperative day the clamps are removed from both loops and double-barrel ileostomy resulted. The wound healed by primary union. On the seventh postoperative day the spur was crushed. Large amounts of intestinal feces were lost through the fistula and the patient rapidly became anorectic. The cranking of the spur did not help to return the fecal stream to normal channels. Catheters and curved glass tubes also proved unsuccessful in obtaining the drainage from the proximal into the distal loop. On the twelfth postoperative day under spinal anesthesia, the fistula was closed by mobilization and end to end anastomosis. The anastomosis was not replaced with the abdomen but was left extraperitoneal beneath the skin. The fistula recurred and the patient's condition became critical. It was decided to do the exclusion operation 7 days prior to this. Miller Abbott tube was inserted into the distal loop for feeding purposes, and to prevent reanastomosis from this loop. This maneuver helped no little in preparing the patient. On March 20, 1930, under local and cyclopropane anesthesia, the exclusion operation (Fig. 3) was performed (I. C. M.). The patient made an excellent recovery, and the wound healed off. The patient was readmitted after 10 weeks, and the blind loops, measuring 5 and 30 centimeters respectively (Fig. 4) are resected under general anesthesia. The defect in the abdominal wall was repaired as for postoperative hernia. Recovery was uneventful, and the patient has since resumed his duties.

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**CASE 3.** M. J. H. an accountant, aged 45 years, developed regional enteritis of the jejunum about 1917. Medical treatment proved unsatisfactory. Surgery in 1921 consisted in entero-enterostomy about the diseased jejunum, and in 1927 the diseased jejunum was resected. Following temporary improvement, enteritis flared up in the terminal ileum. Surgery in 1929 consisted in two stage resection of the terminal ileum and of the right half of the colon. A fistula appeared for the first time subsequent to the second stage, on July 27, 1929. The fistula originated from the inverted end of the ileum, and ran along posterior abdominal wall to terminate in the right flank. The fistula persisted despite local measures, and in January for cure was performed on December 30, 1929. Through right subcostal incision, the tract was excised after it was traced to its origin in

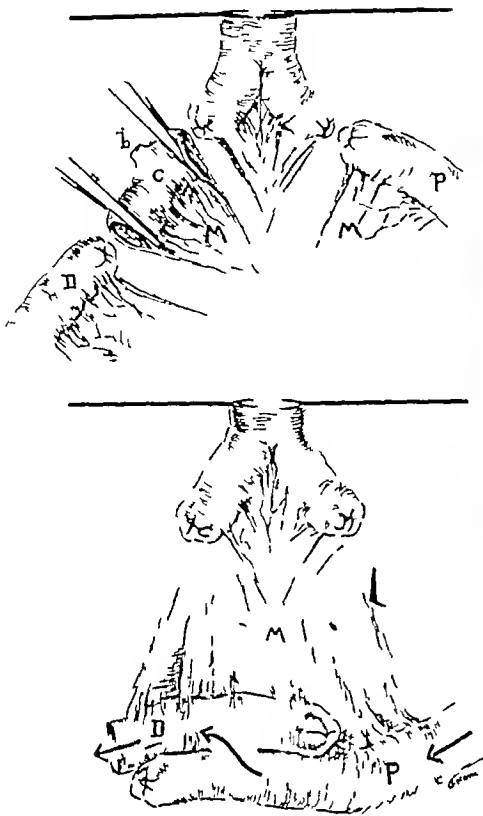


Fig 3 The complete exclusion operation, Case 2 A, above, uncontrollable fistula following exteriorization of gangrenous ileum. Operation begun by resecting segment C because of perforation. B, below, operation completed, fistula entirely excluded. P, proximal and D, distal loops, M, mesentery.



Fig 4 Barium has been introduced through catheters into the two blind loops following their complete exclusion by operation. This figure corresponds to Figure 3B.

Cokkinis recommends a side-to-side anastomosis as a step in the operation of exteriorization of the small intestine for acute obstruction with gangrene. This step he argues will help in closing the subsequent fistula. If side-to-side anastomosis has been performed at the time such exteriorization was carried out, then later closure of the fistula is feasible by invaginating the distal stumps of the intestine and returning them within the peritoneal cavity. This procedure, however, is not always satisfactory, and if it fails, the operation of complete exclusion is recommended.

Given a fistula, side-to-side anastomosis deep to the fistula is sometimes attempted as a step to aid in its closure. The performance of this procedure is hardly any easier than the performance of the complete exclusion operation, and is by no means as satisfactory, because the fecal stream is not completely diverted. If exclusion of any kind is to be recommended for fistula, it should be complete and not partial.

*For acute intestinal obstruction.* The exclusion operation is valuable for the treatment of acute obstruction of the small intestine, because it can effectively control the fistula which invariably follows exteriorization of nonviable intestine. Fistula from exteriorization is difficult to deal with, and is the reason stated by Cokkinis "responsible for the preference which many surgeons show for primary resection and anastomosis." Yet "exteriorization has a much lower primary mortality than the more radical method of immediate resection and anastomosis." The dis-

is done at the outset, and the operator can stop there if he desires. The operation begins with the easy and the important part, namely, the anastomosis. The tedious, relatively unimportant, and often unsterile part of dissecting the fistulous tract down to the intestine and mobilizing the intestine is left to the end of the operation, or to a second stage if so desired.

*3 Operations of the partial type of exclusion.* Near the beginning of this article, the reader was asked carefully to distinguish between complete exclusion and partial exclusion. Partial exclusion, as for instance end-to-side ileocolostomy, is sometimes recommended to treat fistula. It is to be condemned, because the intestinal contents continue to find their way through the fistula, and because spill-over may occur into the blind loop. This loop may distend and cause new symptoms, necessitating its resection or complete exclusion.

would probably have survived the extensive operation of resection of the fistulous segment of intestine with primary anastomosis. In this difficult situation, death was narrowly averted by the use of the operation of complete exclusion.

From this experience of successfully controlling fistulas following exteriorization, it is hoped that exteriorization for gangrene of small intestine may be more widely used in the future. In the past, exteriorization has often been avoided by surgeons because of the extreme difficulty of successfully dealing with the fistula of the small intestine which necessarily follows exteriorization. To avoid fistula of the small intestine surgeons often attempt unwisely to resect gangrenous small intestine which causes acute intestinal obstruction and to perform primary anastomosis an operation which carries a very high mortality often over 50 per cent. With the realization that fistula of the small intestine can be successfully controlled by the operation of complete exclusion, the method of treating acute intestinal obstruction which requires resection of the small intestine may undergo change, and the high mortality of this distressing condition may be lowered.

These remarks, of course, do not apply to the treatment of obstruction of the large intestine, for in such cases the Mikulicz measures are of unquestioned merit.

3. *The one stage operation of excision of the fistulous tract resection of the fistulous segment of intestine and immediate anastomosis.* Any extensive operation would probably not have been tolerated by the 3 patients of this series. The one stage operation of excising the fistulous tract, resecting the fistulous segment of intestine and anastomosis might well have proved fatal. On the other hand the operation of complete exclusion proved safe and was tolerated surprisingly well by these debilitated individuals.

The complete exclusion operation serves actually to break an extensive one-stage procedure into two stages, the first stage being the exclusion operation itself and the second stage being the resection of the blind fistula.

The complete exclusion operation when used to treat fistula attacks the important part first. The anastomosis is performed before the fistulous loop of intestine is resected. The blind loops which lead to the fistula may be dealt with immediately or later as the condition of the patient indicates. This is in contrast with the usual method of dealing with a fistula of the small intestine, in which the incision is usually made down along the fistulous tract, the fistula dissected out, the connecting intestine identified by a tedious dissection and

finally cut away leaving the anastomosis to the last part of the operation. The usual operation proceeds from a dirty field to a clean field whereas the complete exclusion operation begins in a clean field and ends there.

The second stage of such a procedure as this, namely the resection of the blind loops, is optional. Thus the first patient refused resection of the blind loops and lived reasonably comfortably for over a year doing her household duties. These blind loops effectively plug the postoperative hernia which was the original cause of strangulation. For the 14 months since the exclusion operation this patient has been free from strangulation previously she had suffered periodical strangulation. The second patient, on the other hand, was carried through the second stage operation 10 weeks after the exclusion procedure. The blind loops were resected and the hernia through which they protruded closed. Had these two stages been done as one it is doubtful that he could have survived. The third patient has returned to work without resection of the blind loops. He has already undergone six major operations for regional enteritis.

Similar two-stage procedures were employed by Cokkinis and by Ginzburg. Cokkinis performed an exteriorization operation for acute obstruction due to strangulated femoral hernia with gangrene of the ileum being unable to close the resulting fistula, he successfully performed the complete exclusion operation. Ten weeks later he resected the blind loops.

Ginzburg also used the operation of complete exclusion for treating 6 patients with fecal fistula due to terminal ileitis. He later resected the blind loops in some of these cases.

An interesting use of the exclusion operation is illustrated by a patient of Dr. Nathan Womack's. This patient developed a fistula of the ileum following exteriorization of gangrenous intestine. Dr. Womack, being familiar with the operation of complete exclusion performed a left rectus incision with the idea of utilizing the operation. After he had done the anastomosis and excluded the fistulous segment, the patient's condition was so good that he proceeded at once to resect the fistulous loops without waiting to do so at a second stage. The patient made an uneventful recovery.

This mode of using the complete exclusion procedure seems worthy of wide application. It would seem safer, less unsterile, quicker and more flexible than the usual procedure for reasons enumerated several paragraphs back. The operation goes from a clean to dirty field, the anastomosis

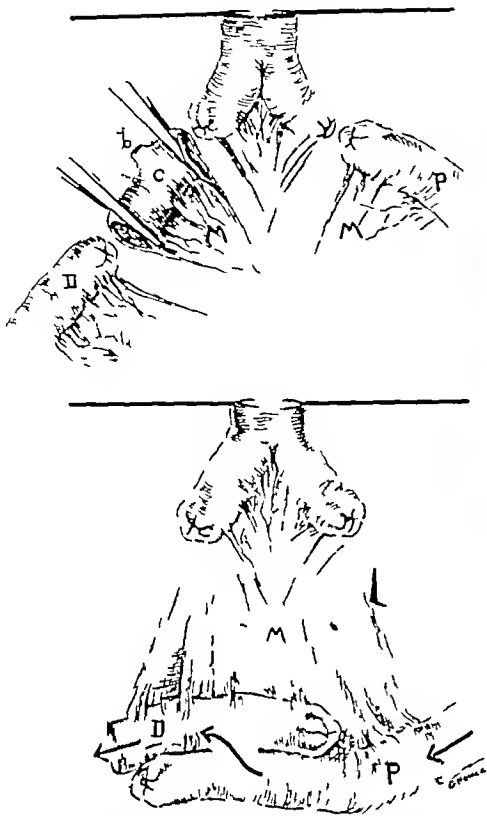


Fig 3 The complete exclusion operation, Case 2 A, above, uncontrollable fistula following exteriorization of gangrenous ileum. Operation begun by resecting segment C because of perforation. B, below, operation completed, fistula entirely excluded. P, proximal and D, distal loops, M, mesentery.



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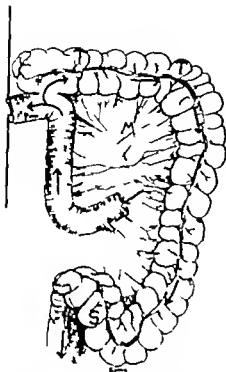
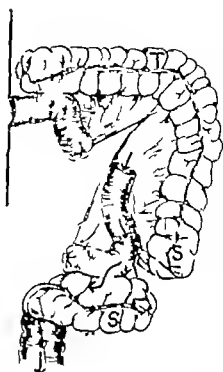


Fig. 3 The complete exclusion operation, Case 3. A, left, uncontrollable fistula following resection of the terminal ileum and right colon for regional enteritis. After suppuration in the unjustified hope of closure by Mikkelsen



stages 3 and 4. B, operation concluded, fistula completely excluded by ileo-cecolostomy. Note that the sigmoid has been cut across and the ends inverted.

advantages of exteriorization are chiefly those incident to fistula, and diminish in proportion to the efficacy of the treatment of fistula.

**Chemical balance.** Restoring blood chemistry to normal before operating for fistula offers certain difficulties. Patients with fistula of the small intestine become debilitated due chiefly to the loss of the external secretions of the pancreas and liver. The proteins of the blood may drop thus in patient 1 the total serum protein fell to 4.8 milligrams per cent and the patient developed nutritional edema just before the exclusion operation was performed. Immediately after the exclusion operation the proteins rose to 6.4 milligrams per cent and edema disappeared.

It is during the period when minor and often ineffective methods are being used in attempts to close a fistula that the blood chemistry is apt to become further altered despite supportive measures such as transfusion, etc. Often, indeed, it is not possible to bring the blood chemistry back to normal without closing the fistula. It seems preferable to perform the exclusion operation early

and thus improve the blood chemistry by restoring intestinal continuity rather than delay in vain hope that the chemistry can be restored before surgery is undertaken. Thus, looking back on the treatment of patients 1 and 2 it is felt that the exclusion operation should have been performed sooner instead of waiting 22 days and 32 days as was done. By so delaying patients 1 and 2 became almost hopeless operative risks.

#### INDICATIONS

The operation of complete exclusion can be used for fistula of the small intestine due to most causes. In this particular series, two of the fistulas were due to gangrene of the small intestine and followed the operation of exteriorization, and the other fistula resulted from terminal ileitis.

The principle of complete exclusion of the intestine is chiefly applicable to fistula of the small intestine although it can be used for the large intestine. It cannot be used for fistula of the duodenum because exclusion of the duodenum

would result in the complete loss of the external secretions of the pancreas and liver, which is incompatible with life

#### CONCLUSION

1 The operation of complete exclusion is recommended for the treatment of certain fistulas of the small intestine

2 Its advantages are (a) it restores intestinal continuity as the first step, (b) it excludes the fistulous segment completely, (c) it is performed in a clean operative field, (d) the operation is surprisingly well tolerated even by debilitated patients

3 The operation proved successful when other measures had failed in the treatment of three debilitated patients with fistula high in the ileum

4 Two of these patients had been operated on for acute intestinal obstruction with gangrene of the small intestine. Exteriorization was used and the resulting fistula resisted closure by all measures short of complete exclusion

5 The third patient had a fistula due to terminal ileitis

6 The operation is not new but its application for fistula is unfamiliar

7 If the operation is more widely used it may possibly cause a reduction in the mortality from acute intestinal obstruction due to gangrene of the small intestine, because it can effectively control the fistula which follows exteriorization

#### BIBLIOGRAPHY

- 1 COKKINIS, A J Postgraduate Surgery Edited by Rodney Maingot Pp 1056-1065 New York Appleton Century, 1936
- 2 DEVINE Quoted by Horsley, J S, and Bigger, I A Operative Surgery 4th ed Pp 898-899 St Louis C V Mosby Co, 1937
- 3 GINZBURG, L Persistent abdominal fecal fistulas due to regional ileitis Surgery, 1940, 7 515-528
- 4 VON HACKER Ueber die Bedeutung der Anastomosenbildung am Darm fuer die operative Behandlung der Verengerungen desselben Wien Klin Wchnschr 1888, 1 359, 389
- 5 SALZER, I Ein Vorschlag zur Modifikation der Entero Anastomose, durch voellige Ausschaltung der Kranken darm Theiles Ber u d Verhandl, d deutsch Gesellsch f Chir, Leipz, 1891, 20 110-121
- 6 TRENDLENBURG Quoted by Guillermo F Muennich Unilateral intestinal exclusion Surg, Gynec & Obst 1923, 36 773-776

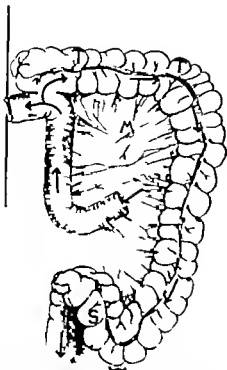


Fig. 5. The complete exclusion operation, Case 2. A, left, uncontrolled fistula following resection of the terminal ileum and right colon. B, regional enteritis. Mark suppuration in the unjustified hope of closure by Mikkelsen.



Fig. 6. The complete exclusion operation, Case 3. A, left, uncontrolled fistula following resection of the terminal ileum and right colon. B, regional enteritis. Mark suppuration in the unjustified hope of closure by Mikkelsen.

advantages of exteriorization are chiefly those incident to fistula, and diminish in proportion to the efficacy of the treatment of fistula.

**Chemical balance.** Restoring blood chemistry to normal before operating for fistula offers certain difficulties. Patients with fistula of the small intestine become debilitated due chiefly to the loss of the external secretions of the pancreas and liver. The proteins of the blood may drop; thus in patient 2 the total serum protein fell to 4.8 milligrams per cent and the patient developed nutritional edema just before the exclusion operation was performed. Immediately after the exclusion operation the proteins rose to 6.4 milligrams per cent and edema disappeared.

It is during the period when minor and often ineffective methods are being used in attempts to close a fistula that the blood chemistry is apt to become further altered despite supportive measures such as transfusion, etc. Often, indeed, it is not possible to bring the blood chemistry back to normal without closing the fistula. It seems preferable to perform the exclusion operation early

and thus improve the blood chemistry by long intestinal continuity rather than delay vain hope that the chemistry can be restored before surgery is undertaken. Thus, looking on the treatment of patients and it that the exclusion operation should have been performed sooner instead of waiting 21 and 33 days as was done. By so delaying treatment and 2 became almost hopeless operations.

#### INDICATIONS

The operation of complete exclusion can be used for fistula of the small intestine due to various causes. In this particular series two of the fistulas were due to gangrene of the small intestine and followed the operation of exteriorization, and the other fistula resulted from terminal ileitis.

The principle of complete exclusion of the intestine is chiefly applicable to fistula of the small intestine although it can be used for the large intestine. It cannot be used for fistula of the duodenum because exclusion of the duodenum

occur, and a severe periodic febrile reaction is not uncommon

The problem of surgical therapeutics in these cases has been one which has taxed the ingenuity of surgeons for over one hundred years. In mild cases, mere support is sufficient, the wearing of a rubber stocking, elevation for part of the day with a restricted activity, permits these patients to continue quite satisfactorily. Mecholyl by iontophoresis, suggested by Irving Wright, has relieved a very limited number in this group. In others, conservative measures are entirely inadequate and, with progression and periodic febrile reactions, many become economic liabilities.

The first operative effort, early in the Nineteenth Century (Les Francke) was with scarification, and Carnochan in 1851 used ligation of the iliac or femoral artery, both of these procedures resulted in many amputations. Dieffenbach and Mikulicz unsuccessfully excised subcutaneous tissues. Handley is credited with the development of the theory of draining obstructed areas through adjoining healthy tissue, using silk sutures as drains. Lang, Walther, Oppel, and Rosenaw all attempted modifications. Kondoleon, observing no lymphatic collections in the muscle, reasoned that the lymphatic blockage was entirely superficial and excised strips of intervening fascia with beneficial effects. Sistrunk, Kimura, Auchincloss, Knudson and Ghormley all added features to this original operative procedure. Homans contends that the beneficial effect of this type of operation is derived only through plastic excision of lymph collections, basing this thought on his failure to find muscle lymphatics and the presence of thrombosis of the iliac lymphatics (Table II).

We believe that much of the success of the operative removal of the superficial and deep fascia in these cases is due to the opening of a new avenue of lymph escape through the muscle lymphatics. Were this not true, the simple excision

of superficial lymph tissue, such as was practiced by Mikulicz and Dieffenbach would have succeeded at times. We have performed biopsies at periods of from 6 to 18 months after this operation, which show a normal arrangement of tissue cells without replacement by lymphatic collections. If the results were due only to a plastic excision of lymph tissue, one would expect some degree of lymphatic accumulation to have recurred in the superficial tissues in this period of time. To augment drainage to contiguous tissues, we have prepared broad base pedicle skin grafts, thus permitting large skin areas to drain to neighboring healthy lymphatic tissue.

In the last 4 years we have performed the outlined operation on 12 patients and in a modified form 6 others have been so treated, and, despite the physiological and pathological processes on which relief is based, we can promise surgically an improvement in a high percentage of cases. Careful pre-operative and postoperative measurements in 6 extremities observed after the radical operation for from 1½ to 3½ years have shown a maintained reduction in the circumference of the leg from a minimum of 7 inches in 1 patient to a maximum of 21 inches in an advanced case, and our most recent patient had the circumference of his calf reduced from 55 inches to 25 inches.

#### TECHNIQUE

1 *Pre-operative preparation* A minimum of 2 weeks' hospitalization is required, during which time the leg is elevated and diuretics, usually in the form of the mercurials, are administered. The fungus infection, which as a rule accompanies this process, is controlled. Sulfanilamide is prescribed prophylactically for several days prior to operation. This drug has been used empirically. Drinker and Fields showed in their work on experimental elephantiasis in dogs, that each time the febrile reaction occurs, streptococci could be cultured from the lymph, and it is in an effort to eliminate these organisms that the sulfanilamide is used. Careful measurements of the circumference of both limbs are recorded. For 2 days prior to operation a careful skin preparation, consisting of green soap and alcohol cleansing and the use of sterile drapes, is carried out.

2 *Operation* Under prolonged spinal anesthesia (pontocaine) an elliptical incision is made in the lateral aspect of the thigh from the iliac crest to the femoral condyle. Below the knee this elliptical incision is continued posteriorly in the calf to its lower margin, when it again runs laterally to the external malleolus. This type of

TABLE II—OPERATIVE RESULTS IN CHRONIC LYMPHEDEMA FROM THE LITERATURE (KONDOLEON PRINCIPLE)

Surgeon	Number cases	Results good	Results fair	Not improved
Kondoleon	6	Not too satisfactory		
Burke	16	6	2	4
Sistrunk	40	30		10
Kimura	9	9		
De Gaetana*				
Torgenson	5	5 (6 months)		
Del Toro & Pons	18	6	6	4†
Kuntzen	16	8	4	3
Ghormley Overton	64 (55 followed)			12 5
	87 5% (56)			(8)

\*Good results with Sistrunk's method  
† not followed.



# THE SURGICAL TREATMENT OF CHRONIC LYMPHEDEMA (ELEPHANTIASIS)

GFRALD H PRATT M.D. F.A.C.S., and IRVING S. WRIGHT M.D. R.A.C.P.  
New York, New York

OF the three circulating media the lymphatic system has been the least thoroughly understood. The arterial circulation, with its visible pulsation its early evidence of failure and its obvious importance to life was the first to be studied. Its corollary the venous system, on which the success of the arterial circulation depends, is anatomically and physiologically more clear. The lymphatic system, with a separate and complete circulation, resembles the venous system in that it eliminates tissue waste products, particularly the ones which the venous system does not remove. It connects with the veins at only two points the important left and the less important right thoracic ducts, which enter the subclavian vein at its junction with the jugular vein. The lymphatic system is of prime surgical importance. Localization, absorption, and tissue response depend upon its adequate function. Surgical cure in malignancy requires the complete excision of the tumor and its primary extent the neighboring lymphatics. The lymphatic system is not only important in

diseases of other organs, but, in itself it may be the site of disease processes. One such pathological syndrome, chronic lymphedema, or elephantiasis, has been a most difficult surgical problem.

Efforts to classify lymphedema on an etiological basis have not been too successful (Table I). To clarify the various groups, a surgical classification based on whether they might respond to surgical intervention has been prepared. The surgical intervention so considered is either local excision or the adaptation of a principle of resection of the superficial and deep lymphatic trunks, with application of the skin directly to the muscles—the so called Koozoleon principle.

The figures indicating incidence of various groups in the last 37 patients with lymphedema registered at the New York Post-Graduate Hospital are as follows:

Shrapnel or precox form	
Chronic phlebitis	20
Varicose vein pathology	6
Familial or atrophic type	
Filaria	
Infection	4
Epidemiophytosis	
Traumatic origin	3

In lymphedema there is an occlusion of the lymphatic vessels, which may be of congenital origin or may be due to pressure, inflammation, or thrombosis. As in other occlusions, fibrosis soon follows, with a permanent closure to drainage through these lymphatic vessels, thus establishing a vicious cycle. This process is accelerated by an increased protein content, which the work of Drinker and Fields and Romans demonstrated to be as high as 4 per cent, or one half that of the blood. The lymph accumulates in the tissue spaces of the involved area, with no method of escape. Elevation permits it to pass through the tissue spaces, to the contiguous normal area where it is removed by unaffected vessels. Dependency causes repeated collections and with the increasing distention, the size of the affected limb increases. The leg becomes swollen, indurated, with pitting edema, and frequently secondary venous changes occur. The subcutaneous tissues become lymph spaces, ulceration may

TABLE I—SURGICAL CLASSIFICATION  
OF LYMPHEDEMA

- I. Amenable to surgical treatment
  - Modified Koozoleon procedure (as presented)
    - Idiopathic
      - Precox
      - Congenital or familial (Atrophic)
    - Acquired
      - Trauma (accidental or surgical)
      - Filaria
      - Infection
    - Occasionally the group secondary to various pathology
  - Local surgical intervention
    - a. Pressure—growth, etc.
    - b. Traumatic or operative scars
    - c. Most venous obstructions
    - d. Local inflammation
    - e. X-ray radium and other burns
    - f. Congenital lymph collections (Cystic hygroma, etc.)
- II. Not Recommended for surgical treatment
  - Mild atrophic lymphedema
  3. Fungal infection
  4. Malignancies with invasion
  5. Allergic or systemic lymphedema

From the Surgical and Vascular Services of New York Post-Graduate Medical School and Hospital (Columbia University)

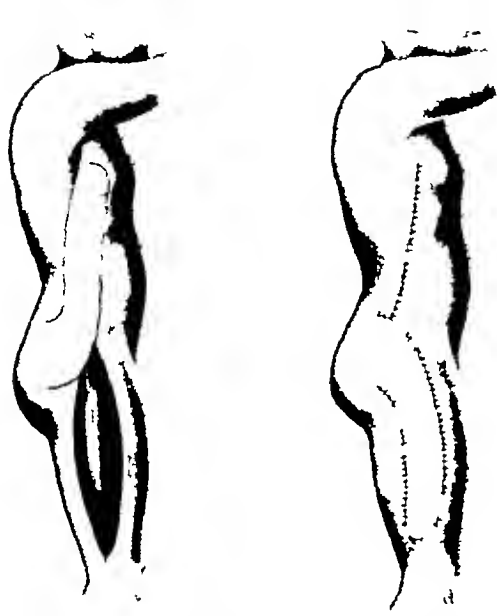


Fig. 4. The broad base pedicle skin graft is used to replace excised diseased skin. Skin lymphatics may thus drain through the broad base to contiguous healthy tissue.

illustrates in cross section by the dotted lines the tissue excised and remaining after the plastic closure. In our latest cases we have removed

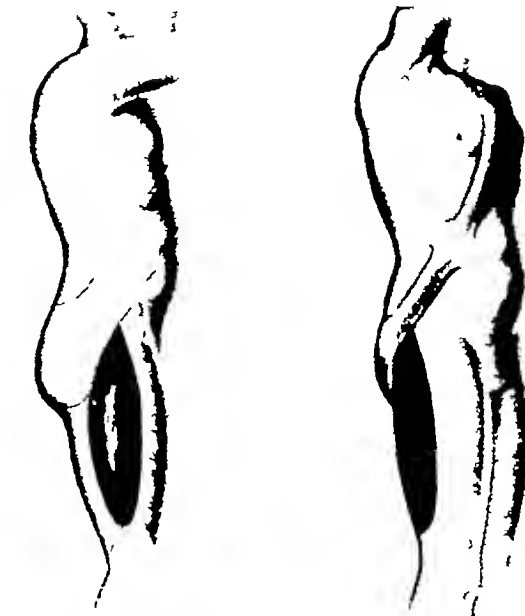
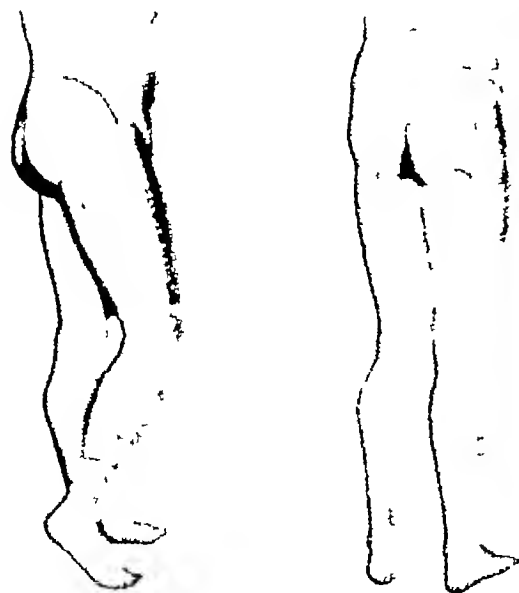


Fig. 5. Broad based pedicle tube graft being prepared with the base in the buttocks above the area of skin lymphatic blockage.

100 per cent of the fasciæ—thus entirely encircling the limb.

In instances in which the skin had become devitalized by constant overstretching it was necessary partially or completely to remove it. The split and full thickness skin grafts, which were



Fig. 7. Left. Preoperative photograph of a patient with chronic lymphedema of the legs. Right. Postoperative photograph of the same patient after removal of the diseased skin and replacement with a split thickness skin graft. The legs are now normal in size and color.

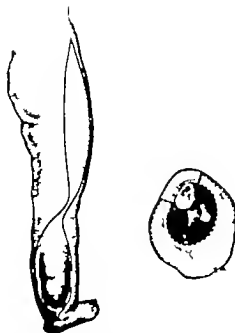


Fig. 1. Outline of incision. The skin is undermined for 75 to 80 per cent of the leg's circumference. The superficial and deep fascia with the outlined skin is removed *en masse* from 5 to 60 per cent of the leg. Cross section shaded area outlined by dots shows section of skin, superficial and deep fascia to be removed.

Incision exposes the area of greatest lymph collection (Fig. 1). In selected instances the incision is modified to run entirely laterally (Fig. 2).

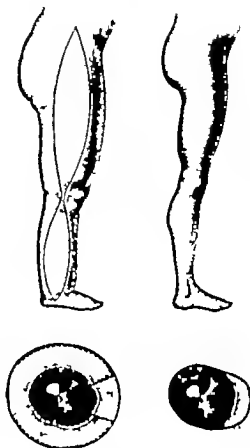


Fig. 2. Alternate incision showing leg outline before and after operation. Cross sections illustrate area to be excised and re-application of skin directly to the denuded muscles.

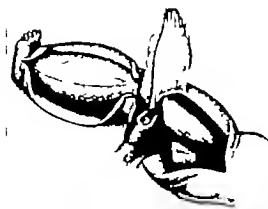


Fig. 3. Outlined skin, superficial and deep fascia being removed *en masse* from two-thirds to the total area of the leg.

A sufficient ellipse is incised to allow the residual skin when approximated, to equal the circumference of the normal limb. The skin alone then is undermined until three-fourths of the circumference of the leg has been exposed; this is done without transverse incisions, which could produce further scars. The incision is then carried through the superficial tissue and the deep fascia throughout three-fourths of the circumference of the leg and a block of tissue which includes the ellipse of skin and the three-fourths circumference of the superficial and deep fascia, is excised *en masse*. Bleeding is controlled, the skin is then united with interrupted alloy steel wire and directly approximated to the denuded muscle. The insert in Figure 1 and Figure 2

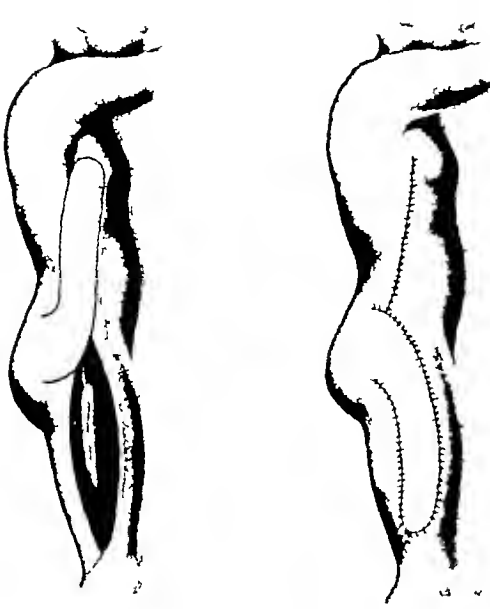


Fig. 4 The broad base pedicle skin graft is used to replace excised diseased skin. Skin lymphatics may thus drain through the broad base to contiguous healthy tissue.

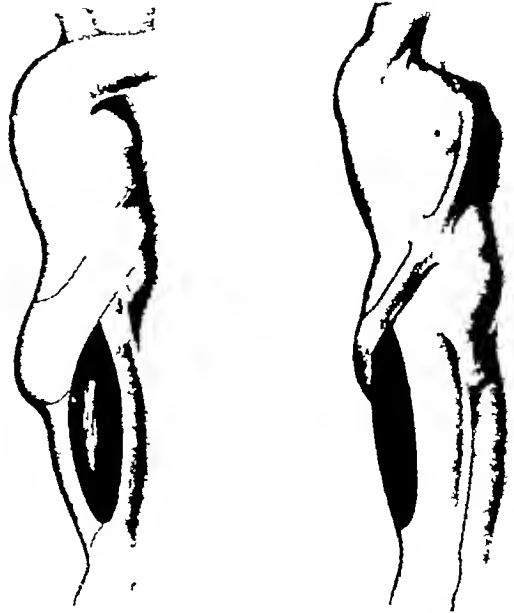


Fig. 5 Broad based pedicle tube graft being prepared, with the base in the buttocks above the area of skin lymphatic blockage.

illustrates in cross section by the dotted lines the tissue excised and remaining after the plastic closure. In our latest cases we have removed

100 per cent of the fascia—thus entirely encircling the limb.

In instances in which the skin had become devitalized by constant overstretching, it was necessary partially or completely to remove it. The split and full thickness skin grafts, which were

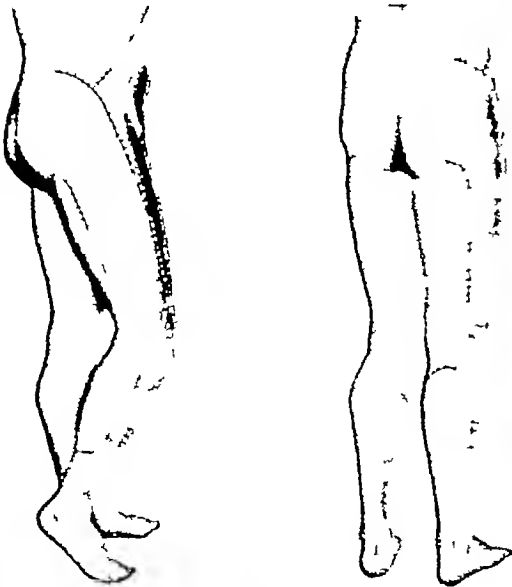


Fig. 6 First figure shows the graft in place, and second figure after plastic operation to complete leg extension.

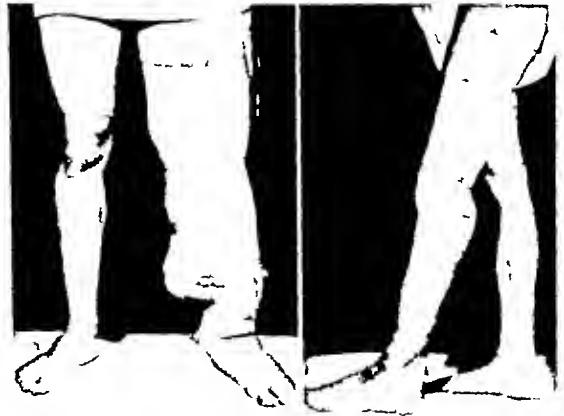


Fig. 7, left. Pre-operative photograph of a male, aged 21 years, with congenital lymphedema. Leg circumference before elevation 37 inches.

Fig. 8. Same patient 3 months after operation. 1 of low up of 1 year shows reduction in leg circumference maintained despite active daily work.

first used were replaced by the more satisfactory broad based pedicle tube grafts. It was found then that in addition to skin replacement, the pedicled graft would drain the skin lymphatics and thus have a new method of aiding skin lymphatic drainage. Inasmuch as the tubes are made 5 inches in width, the drainage factor becomes an important one. This skin graft, as shown in Figures 4 and 5, is an important addition to the operative treatment.

3 *Postoperative care* The limb is maintained in an elevated position for approximately 3 weeks, after which time the patient is gradually permitted to lower the leg and bear weight, always with support. When necessary the secondary plastic operation after the graft is performed. After-care consists of support for 6 months, when the bandages may be removed gradually dependent upon swelling. It is well to emphasize the fact that this is a chronic circulatory disease and that subsequent support at times may be found necessary.

#### POINTS TO EMPHASIZE

We would emphasize the careful selection of the patient, the pre-operative preparation, spinal anesthesia as the anesthetic of choice, the measuring of the circumference of the leg, the radical undermining of at least three-fourths of the circumference of the leg, care to prevent constriction at the joint, and the use of steel wire to reduce resection. Our more recent work with the broad base pedicle skin graft to replace the widely excised diseased skin seems even more satisfactory. Blood transfusion has reduced the incidence of operative shock. By being sufficiently radical a second stage operation on the opposite side of the leg has been eliminated. In only one instance has there been a slough and that was over the dorsum of the foot, where the desire for a better cosmetic result caused too great undermining. This had a recurrent lymphedema, and the previous scars were a factor. The deep fascia had regrown since a previous, much less radical, operation at another institution 5 years before.

# EDITORIALS

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## SURGERY Gynecology and Obstetrics

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FEBRUARY, 1941

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### THE DECREASING MORTALITY OF APPENDICITIS

SO much has been written and said about the increasing mortality of appendicitis that such statements have been accepted widely. But if the latest figures available are examined closely, some doubt arises about the validity of this conclusion. According to the figures compiled by the United States Bureau of the Census, the death rate from appendicitis has decreased progressively and significantly from 1930 to 1937,—the last year for which figures are available. The reported mortality rate of appendicitis per 100,000 population in the United States was 15.3 in 1930, 15.2 in 1931, 14.2 in 1932, 14.1 in 1933, 14.3 in 1934, 12.7 in 1936, and 11.0 in 1937, or a reduction of 28.7 percent in seven years! According to the statistical bulletin of the Metropolitan Life Insurance Company, this trend continues.

Moreover, if the figures prior to 1930 are analyzed critically, there is considerable evidence to show that the incidence and the

mortality rate from acute appendicitis have remained stationary or at least have not been increasing for an even longer period of time.

Perhaps one of the most careful and most widely quoted compilations of the death rate of acute appendicitis is that of Hoffman, which appeared in the *Spectator* in 1933. He concluded that in the *sixty largest cities of the United States* the appendiceal death rate has been increasing. For the country as a whole, however, in 1933, Hoffman says, "For all practical purposes the death rate has reached a stationary condition with a slight tendency downward." The death rate in the *sixty largest cities* had increased but this is not, however, in our opinion, a true index for the country as a whole. It does not take into consideration the enormous increase in hospital facilities and the even greater increase in the number of patients hospitalized, in the last fifty years. According to figures compiled by the American Medical Association there were fifty thousand hospital beds in the United States in 1872. In 1909 there were 421,000, in 1918, 612,000, in 1928, 892,000, and in 1937, 1,124,000—or a twenty-fold increase in 55 years. Hospitals are located in the larger cities, but the patients who occupy hospital beds may come from the city itself or the surrounding countryside, and the number of deaths reported from hospitals may represent a much larger area of population than the cities reporting. Just because more people die from appendicitis in the hospitals of the *sixty largest cities of the United States* (which is correct), may not, or necessarily indicate that the incidence and mortality of appendicitis are increasing in the United States as a whole. It may mean only that more people go to the hospital each year. In

deed, the ratio of the total number of patients admitted with appendicitis to the total number of hospital admissions has decreased.

Prior to 1930 the reported mortality rate from acute appendicitis increased from 9.7 per 100,000 population in 1900 to 15.3 per 100,000 in 1930. These figures might reflect any one or a combination of more than one of three separate and distinct trends: i.e. more accurate diagnosis, increased fatality rate or increased incidence of appendicitis. From the evidence at hand it would seem reasonable to assume that more accurate diagnosis has played a major rôle in almost doubling the reported death rate of appendicitis, from 1900 to 1930. Not only has medical diagnosis become more accurate during these years, but the average patient has had more adequate medical attention coincident with the shift in population from rural to urban areas. Diagnosis has been further facilitated by this great increase in the number of patients hospitalized during this period, with the increased opportunity for consultation, laboratory procedures, and particularly postmortem examination which hospitals offer.

Then too education of the medical profession to recognize appendicitis except in the large medical centers was slow so that deaths from this disease were either erroneously classified or included in the group "Death from unknown or ill-defined causes." Even today in certain isolated sections of the country "Inflammation of the bowels is a more popular diagnosis than acute appendicitis." In any event while the reported death rate from appendicitis increased only 5.6 per 100,000 population from 1900 to 1930 the reported death rate from unknown and ill-defined causes decreased from 73.8 per 100,000 population in 1900 to 21 per 100,000 in 1930. In other words from 1900 to 1930, 52.8 deaths per 100,000 population or almost ten times the

increase in the number of deaths attributed to appendicitis were removed from the category of "Unknown and ill-defined causes and correctly classified. As those 'unknowns' were reclassified the number of deaths assigned to every other cause was increased, and it seems reasonable to assume that the relatively new and unfamiliar disease "appendicitis" was a major recipient.

In any event, the mortality rate from appendicitis in the United States as a whole has not increased but has decreased significantly in the past 10 years. And although we do not believe the present record to be an ideal one we are encouraged to note this significant reduction in the ravages of "intrapentoneal enemy number one" and we feel confident that this trend will continue due to the continued campaign for education of the lay public and the continued campaign for improvement in the standards of surgical and hospital care.

WOOLFOLK BARROW

## LOCAL TREATMENT OF THE BURNED AREA

*It is balsam anointed De Quisole, the receipt of which I have in my memory, with which one need have no fear of death, or dread dying of any wound.*

*If that be said S. nich. Panto, of renouance beneath the government of the promised island, and desire nothing more I payment of my men and faithful services that your worship give me the receipt of this prime liquor*

**D**ESPITE a great amount of careful experimental study and clinical observation the problem of the nature of burn toxemia is still unsettled. There is no general agreement as to whether there is a burn toxin and if there is, as to its nature and still less agreement as to the source of the toxin if we concede for sake of argument that such a product is present. Efforts directed toward the local treatment of a burn based upon the assumption that the source of

the burn toxemia is the burned tissues met with such an improvement in results that the conclusion seemed almost inescapable that the premise must be correct. Davidson's tannic acid therapy for burns has become universally adopted. When carried out as advocated and as has been repeatedly stressed by such men as Penberthy and McClure who had close contact with Davidson, the treatment yields most excellent results.

However, observations of many cases treated with tannic acid without the careful preliminary cleansing stressed by the originator of the method have shown that disastrous results may follow. It has become obvious that simply to coagulate the dead protein of the burned surface is not enough but that some other factors are important. Various antiseptics or rapidly tanning agents have been added to, used in conjunction with, or substituted for, tannic acid, but none has been more successful than tannic acid.

It is instructive to disregard for the moment those factors in burns about which our knowledge is incomplete and to look upon a burn simply as a large open wound in which the tissues are badly damaged and seriously handicapped both in reparative powers and in resistance to bacterial invasion. Associated with such a wound we would also anticipate shock, a phenomenon as perplexing as that of burn toxemia but for which we have certain fairly satisfactory methods of treatment. I mention the question of shock only to complete the analogy between burns and other open wounds.

Let us follow such an injury from the time of its inception to that of its definitive care, forget that we are dealing with a burn, and simply think of the injury as a large open wound which is receiving the care so often accorded a large burn. When this injury occurs, it is usually under circumstances of great

flurry and excitement. The patient, fully clothed, often with the wounded area and covering clothes soiled, sustains a painful injury into which dirty clothing and contaminants from the skin are immediately deposited. Someone, in order to stop the action of the traumatizing agent, may roll the victim in a rug or some other contaminated material. Unless the wound is too serious, a well meaning friend or neighbor or parent smears the surface with butter or soda or lard or one of the various proprietary ointments recommended in advertisements for first aid treatment for burns. The patient is then brought to the hospital in an ambulance, often wrapped in another blanket and is deposited in the emergency room. From the time of the injury to the arrival in the emergency room, the wound has been taken care of by one or more individuals none of whom is masked and all of whom have directly or indirectly contaminated the raw area with unsterile hands, expired droplets, ointments, and dressings. In the emergency room, the wound is uncovered and examined by several persons. If there is no apparent shock or if the shock is not too marked, a hypodermic of morphine is administered and treatment of the wound is started. Masks and caps and sterile gloves are usually lacking. The clothes are cut from the patient, and the wound is exposed and again examined. Adherent dressings and clothing are picked off, and the raw area is then covered with another ointment or preparation is made for tanning it. If it is to be tanned, the patient is placed on a sterile sheet, a light cradle is placed over him, and someone delegated to spray the area with tannic acid solution every 20 to 30 minutes until "done." This process may require 12 to 24 hours during which time the open wound is exposed to the air, partially protected from contaminants by the coverings of the light cradle and by a crust



which rapidly becomes impervious but is still subject to cracking with consequent exposure of the surface. If cracks appear in the crust even after 24 to 48 hours, the spray is again used on them and the area is again tanned. Where ointments have been used, dressings are applied over them and these are removed daily or every few days to allow the re-application of more of the magic salve.

If we look upon this injury as an open wound forgetting that it is also a burn, we are not surprised to learn that a very high percentage of victims develop serious infection, that the wounded areas take weeks and months to heal and that mortality rates tend to be very high. Nor are we surprised if secondary contamination occurs during the frequent dressings which usually mark the course of an extensive burn.

In this theoretic imaginary wound one factor which has been insufficiently considered is that of the contamination of the large raw surface. The aim has been to cover it with *something* as rapidly as possible ignoring the fact that the surface is already liberally contaminated with dirt and bacteria, and is susceptible to further contamination with bacteria from the nose and throat of everyone who examines it. To treat such a wound without first thoroughly cleansing it violates not only the principles of good surgery and the tenets laid down by Davidson but also speaks for a faith in tannic acid or some well advertised ointment exceeded only by that evidenced by Don Quixote in the balsam of Fierabrax.

Let us disregard for the moment any conception whatsoever concerning burn toxins and simply conceive of a burn as a large open wound. Our ideas concerning its management at once change and our initial efforts in dealing with it are directed toward cleansing the surface of as many contaminants as possible of removing as much debris as can be removed

and of covering the area as quickly as possible with a sterile protective dressing. The burn may be cleansed as any other open wound with soap and water and liberal flushings with normal salt solution. While this is being done every possible precaution is taken to prevent bacteria from nose and mouth and other objects from gaining entrance to the wound. Caps and masks should be worn by every one who takes part in the cleansing or who comes into the room during the process. As strict an aseptic technique should be followed as in the operating room. Hands should be scrubbed and covered with sterile rubber gloves. Instruments and dressings should be sterile and an attempt made to complete the cleansing and dressings at the earliest possible moment. As for the coverings for the wound there are only two prerequisites: first, that they be non-irritant and second, that they adequately protect the surface and prevent fluid loss from it. A large pressure dressing similar to that applied over skin grafts seems to be advantageous in that it helps to immobilize the part and minimizes the loss of fluids into the tissues about the burn. If the burns affect the extremities, splints should be used to provide rest for the injured part while for burns of the trunk we would rely mainly upon nature's efforts to splint it. The shock that accompanies such a wound and the protein and electrolyte imbalance that may occur may be controlled by the usual measures of warmth and sedation, and the administration of fluids in the form of blood or plasma transfusions, saline and glucose.

If this conception of a burn as a wound is correct it should not matter much just what the covering agent is. If we can get the raw surface quickly covered with a tannic crust and not expose the wound for too long a time while doing so and keep the crust from cracking or constricting or traumatizing the skin at

its borders, we will have a satisfactory dressing. If there is available some other type of dressing which is more rapidly applied and does not have the disadvantages of a brittle crust, there should not only be no reason for not using it but certainly definite advantages in doing so. Equally admissible should be the conclusion that the burned area is a raw surface susceptible to contamination for as long a time as it remains open. Dressings subsequent to the one applied following the initial care should, therefore, be reduced to a minimum in number and should be carried out with strict aseptic technique. The use of unsterile salves and irritant chemicals would find no more application in the burn than in a compound fracture.<sup>1</sup>

<sup>1</sup>In the children's wards at Cook County Hospital in Chicago the mortality rate from burns has been reduced from 10 per cent to 3.9 per cent by a method of treatment such as that which is outlined here. Careful soap and water cleansing, and a pressure dressing over vaseline gauze (personal communication Dr. Harvey S. Allen).

It has seemed to me that the emphasis in the care of burns were better placed on their character as open wounds than on some agent which is to be applied to the surface. Davidson's great contribution to surgery, namely the demonstration that a burn may be cleansed and closed the same as any other open wound, has been transformed into a plea for tannic acid. If it appears that closure may be more effectively accomplished, after careful soap and water cleansing, with simple sterile vaseline strips and large amounts of dry gauze snugly bandaged over the burn, it does not detract a whit from the monumental contribution made by Davidson. It is the principles that count in surgery, and if they can be shown to apply to burns as they do to the treatment of any other open wound, a tremendous service has been rendered.

MICHAEL L. MASON

# TEXTS AND DOCUMENTS

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**E**VEN the medical man who is a staunch adherent of Methodism is probably unfamiliar with the fact that the Rev. John Wesley wrote a book on medicine. According to Arnold Lunn, one of his biographers, John Wesley, distrustful doctors, and was never happier than when prescribing for his friends. "I thought, he says, of a kind of a desperate experiment. I will prepare and give them physic myself. The book published first in 1747 is entitled *Primitive Physic or An Easy and Natural Method of Curing Most Diseases* by the Rev. John Wesley A.M. Late Fellow of Lincoln College, Oxford. His suggestion that "*The Primitive Physic* should be in every family" was with his other literary output for his followers tantamount to a command to buy. Best seller Wesley made a lot of money from his literary output which money was given away.

The command to buy his books probably accounts for the numerous editions of his *Primitive Physic*. The twenty-eighth edition of this book, a small duodecimo volume of 103 pages was published at London in 1855 and sold by Blanchard, 24 City Road and at the Methodist Preaching Houses in town or country.

The original preface to the work of 1747 is repeated with a postscript dated 1755 and two subsequent introductory remarks with respect to additions and corrections dated 1760 and 1780, respectively. It is from this twenty-eighth edition that excerpts are taken as items of interest in this curious book designed as guide to families experiencing sickness or diseased conditions. This volume on domestic medicine was treated analytically by George Dock.<sup>8</sup> This is decidedly not my intention. Having been serious for the most part, in this series, I thought it time to introduce something that would amuse the modern physician and by direct quotation cause him possibly several chuckles. The body of work is arranged in ency-

clopedic (alphabetical) form beginning with "Abortion" 149, "St. Anthony's Fire and ending with Emetic Tartar 150. "Water Drinking, but the last subtitle lists out of alphabetical sequence, *Electrifying, and Fasting Spittle*.

The last sentence is a "plug" for he advises "all, in or near London, to buy their medicines at the Apothecaries Hall. There they are sure to have them good.

Quoting general health rules from Dr. George Cheyne he gives receipts for various ailments some of which, to inspire confidence of the reader in their effectiveness, he marks with an asterisk. The ensuing quotations from this book are repeated for their curious and perhaps mirth producing quality.

"Malt liquors (except clear small beer or small ale, of due age) are extremely hurtful to tender persons.

"But I still advise in complicated cases, or where life is in immediate danger let every one apply to a Physician that fears God. From one who does not, be his fame ever so great, I should expect a curse rather than a blessing.

"For an Ague Apply to the stomach a large Onion slit."

"To cure Baldness. Rub the part, morning and evening, with onions, till it be red and rub it afterwards with honey. Or wash it with a decoction of boxwood. Tried. Or electrify it daily.

A Cancer in the Breast. Take Horse Spurs (warts that grow on the inside of the horse's forelegs) and dry them by the fire, till they beat to powder. Sift and infuse two drachms in two quarts of ale. Drink half a pint every six hours, new milk warm. It has cured many. Tried. Or, apply goose dung andcelandine, beat well together and spread on a fine rag. It will both cleanse and heal the sore.

Children. No child should touch spirituous or fermented liquor nor animal food, before two years old.

"For Chln Cough or Hooping Cough rub the back lying down with old Rum. It seldom fails.

John Wesley. By Arnold Lunn. The Dial Press, New York 1920. Longmans Green & Co. Toronto.

8. *The Primitive Physic* of Rev. John Wesley. By George Dock, M.D., J. Am. M. Ass. 1915, 61, 629-633.

"For Consumption Turn a pint of skimmed milk with a half a pint of small beer Boil in this whey about twenty Ivy leaves, and two or three sprigs of hyssop Drink half over night, the rest in the morning Do this, if needful, for two months daily This has cured in a desperate case Tried "

"For dull sight drop in two or three drops of juice of rotten apples often "

"For 'iliac passion' meaning 'a violent kind of cholic in which the excrements are supposed to be thrown up by the mouth in vomiting' [fecal vomiting in acute intestinal obstruction or appendicitis?] —

"Hold a live Puppy constantly on the belly (Dr Sydenham) "

"For Sore and Running Legs Poultice them with rotten Apples Tried But take also a purge or two every week "

"Quinsy may be treated by applying a large White Bread Toast, half an inch thick dipt in brandy, to the crown of the head, till it dries "

"For stitch in the Side apply Treacle spread on a hot Toast Tried "

"Use no violent diuretics for 'Stone ' Mead is a proper drink "

"To Stop Vomiting Apply a large Onion slit across the grain to the pit of the stomach Tried "

Dr Wesley's book ends with the marvelous efficacy of "fasting Spittle" when outwardly or inwardly applied When outwardly applied it has relieved or cured "blindness, corns, fresh cuts, deafness, scorbutic tetter, sore legs and warts " Given inwardly it relieves or cures "asthmas, cancers, falling sickness, Gout, gravel, palsy, scurvy, stone and swelled Liver "

Enough has been cited to indicate the curious character of the Rev Wesley's therapeutics, more will occur to the contemplative reader in connection with Wesley's reference to the use of ale, rum and mead

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

WHEN in a volume there converges thorough scholarship, seasoned experience and a gift for clear prose the happy result is a textbook such as *Diseases of the Nervous System*. That labyrinth which constitutes clinical neurology is here illumined in such a manner that beginner in addition to assimilating the material might even find it palatable.

The opening chapters give an adequate review of the anatomicophysiological considerations necessary for the understanding of neurologic function and dysfunction; then the various disease entities are described in a systematic and pithy fashion. This edition includes discussions of recent developments in neurology such as the psychological manifestations of organic disease, electro-encephalography and the rôle of vitamin deficiency in nervous disorder. Other topics of timely interest deal with the neurotropic viruses and the chemistry of muscle and humoral factors in the transmission of nerve impulses at the myoneural junction.

This work is undoubtedly one of the best textbooks of neurology extant. Its usefulness is not exhausted with the beginner; graduate student, teacher and practitioner will all find it a clear and

succinct guide to their experiences in clinical neurology.

HARRY A. PETERS

IN a previous publication in textbook form, Dr Hugo Rosenthal has set forth the theory and practice of radiology of the cardiovascular system, giving a number of short case reports as examples. The present atlas of 25 pages of 3 inch size and 166 illustrations presents a comparative study of the roentgen and the postmortem findings. Stress is laid upon the changes in form and structure of the heart, the great vessels, and the lesser circulation as revealed by the x-ray studies. The case reports include many types of disease but particularly the most common cardiovascular affections. The presentation correlates the roentgenological method with electrocardiography, ophthalmoscopy and the clinical and laboratory studies. Particularly helpful are the large size cuts, many of them clarified by line drawings and photographs of whole specimens and of sections. The workmanship of the book merits high praise. It is really a pleasure to study a book whose illustrations are, in the first place, so beautiful and excellent and, in the second place, so beautifully reproduced in the text. This is a very satisfactory publication.

JAMES T. CASE

*DISEASES OF THE NERVOUS SYSTEM*. By W. Russell Bruce, M.A., D.M. (Oxon.), F.R.C.P. (Londn.) and ed. London: Oxford University Press, 1940.

*ATLAS OF CARDIOVASCULAR RADIOLOGY*. By Hugo Rosenthal, M.D. F.A.C.P. Brooklyn, N.Y. and Baltimore, Md.: Charles C. Thomas, 1940.

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

*FOREIGN BOOKS LEFT IN THE ARCADES: THE SCHEMATIC PROBLEMS OF THE LOCAL PROBLEMS*. By Harry Sturgeon Cromer, M.D., and David Frederic Cromer, LL.B. St. Louis: The C. V. Mosby Co. 1940.

*LEPTODERMIS: DISEASES OF THE CUTANEOUS LIPID METABOLISM*. By Siegfried J. Thannhauser, M.D. Ph.D. Edited by Henry A. Christian, A.M. M.D. LL.D. Sc.D. (Hon.) F.A.C.P. Hon. F.R.C.P. (Can.) Reprinted from Oxford Loom-Leaf Medicine. London, New York, Toronto: Oxford University Press, 1940.

*THE ENDOCRINE FUNCTION OF LIVER*. By William Thomas Salter. Cambridge, Mass. Harvard University Press, 1940.

*DIAGNOSIS AND THE THEORY OF MENSTRUAL DISORDERS AND STERILITY*. By Charles Martin M.D. F.A.C.S. and

S. Leon Jurell, M.D. F.A.C.S. New York and London: Paul B. Hoeber, Inc. 1940.

*A FAMILY DOCTOR NOTEBOOK*. By I. J. Wolf, M.D. New York: Fortune's, 1940.

*THE CURRENT IN GENERAL PRACTICE, SURGERY (Continued)*. Articles reprinted from the *British Medical Journal*. Vol. 4. London: H. K. Lewis & Co. Ltd. 1940.

*THE MEDICAL MANUAL OF THERAPEUTICS AND MATERIA MEDICA*. 7th ed. Rahway, N. J. Merck & Co. Inc. 1940.

*I SEARCH OF COSMOPOLITANISM: An autobiography by Eugene de Savitch, M.D.* Foreword by Arthur Kropp. New York: Simon & Schuster, 1940.

*A SURGEON EXPLAINS TO THE LAYMAN*. By M. Newmoe, M.D. New York: Simon & Schuster, 1940.

*DIAGNOSIS AND THE THEORY OF ASTHMA: ALLERGIc DISORDERS*. By H. M. Marple, M.D. M.S. F.A.C.P. New York and London: Paul B. Hoeber, Inc. 1940.

*CLINICAL PHYLLOXERA*. By Seale Harris, M.D. *Amateur*. By Seale Harris, J. M.D. Foreword by E. V. McCulloch, Ph.D. Sc.D. LL.D. St. Louis: The C. V. Mosby Co. 1940.





# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 72

FEBRUARY 15, 1941

NUMBER 2A

### ASEPTIC RESECTIONS IN THE GASTRO-INTESTINAL TRACT

*With Special Reference to Resection of the Stomach and Colon*

OWEN H. WANGENSTEEN, M.D., F.A.C.S., Minneapolis, Minnesota

**S**ATISFACTORY methods of establishing intestinal continuity after resection by the closed or aseptic method have been available for over 30 years. It is only within the last decade, however, that the closed method of anastomosis has acquired converts in any numbers. The Parker-Kerr (1908) basting stitch excited the interest of a number of American surgeons in the closed methods of intestinal anastomosis, and the growing concern displayed by surgeons in the past decade in aseptic anastomoses may in a sense be said to be cumulative. The development of special clamps to facilitate performance of the anastomosis by Rankin and Stone have accelerated considerably wider acceptance of the closed method.

Yet, within the past year, two well-known American teachers of surgery fathered a textbook on operative technique and failed to describe the closed method of anastomosis. This occurrence, I believe, mirrors fairly accurately

the attitude of a large body of surgeons toward the closed anastomosis. A few surgeons, while insisting that the closed anastomosis be employed in establishing intestinal continuity after resection in the colon, feel no necessity for employing the same method in establishing intestinal continuity in the small bowel. A larger number cling to the open anastomosis just as they embrace all the worthwhile traditions of the past. A number of those, however, who are in a position to influence the opinions of others are inclined, I fear, to look upon the closed anastomosis as an unnecessary refinement or perhaps even as the figment or fetish of surgical dilettantes. Those familiar with the advantages and niceties of the closed anastomosis recognize that the method meets fully the requirements of clean, exacting surgical technique, embodying sound principles of architectural reconstruction. Those who scoff at the closed or aseptic anastomosis need our compassion more than they deserve our censure, for they are probably unaware that they, like the open anastomosis, are sliding backward, perhaps imperceptibly, yet definitely.

My apostasy from the open method of anastomosis is relatively recent, though for more than 2 years I have made only closed anastomoses in the gastro-intestinal tract. I confess freely that my enthusiasm for the closed anas-

From the Department of Surgery, University of Minnesota Medical School, Minneapolis.

Presented before the Clinical Congress of the American College of Surgeons, Chicago, October 21-25, 1940.

The researches presented here were supported by grants of the Graduate School of the University of Minnesota. The Augustus L. Searle Fund for Experimental Surgical Research, the Committee on Scientific Research of the American Medical Association, and by a grant for technical assistance by the Works Projects Administration. Official Project No. 665 71 3 69 Sub-Project No. 58.





*Evans A. Graham*

PRESIDENT 1940-1941

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tomosis may partake of the zealous fervor of a proselyte for his new sect. Yet an enlarged experience has not diminished this ardor but, on the contrary, has strengthened the conviction that satisfactory continuity after segmental resections can be established in the gastro-intestinal canal with less risk to the patient by the closed than by the open method of anastomosis.

#### THE TECHNIQUE OF CLOSED ANASTOMOSIS

Somewhat more than a year ago I described a method of closed anastomosis adaptable to any segment of the alimentary canal. It was proposed in particular to describe a technique for establishing gastrojejunal continuity by the closed method following gastric resection. Satisfactory anastomoses employing the method have been made between the esophagus and jejunum, stomach and jejunum, as well as between segments of small intestine and colon. The method is adaptable to end-to-end, end-to-side or side-to-side anastomoses. The instrumentarium and technique are simple though the latter is, of necessity, somewhat more precise and exacting than that of the open anastomosis. The time consumed in making the anastomosis, particularly the gastrojejunal anastomosis, is somewhat longer than that of the open operation in which running sutures are employed largely—a consideration declared by some surgeons to be of great importance but a matter which, as far as my experience goes, is of no consequence to the patient, whose interest in the operation is to be regarded as paramount.

The technique of anastomosis is essentially the same no matter what tubular segments are to be approximated. Briefly told two rows of interrupted sutures are placed posteriorly the most posterior row being placed first and the interrupted plain quilt mattress suture of Halsted being used. The suture nearest the clamp both behind and anteriorly is of the Cushing variety. Finally a row of Halsted mattress sutures is placed anteriorly completing the anastomosis.

The advantage of the instrument described by the writer patterned after the Martzloff intestinal clamp is that it provides the superiority and adaptability of two clamps for the

posterior row permitting rotation of the clamps as becomes necessary in accomplishing the approximation. A ferrule is applied to the distal end of each blade (Fig. 9) as the instrument is closed to insure and maintain satisfactory coaptation of the thin jaws of the clamps. On completion of the two posterior rows of sutures the two clamps are then rotated in an axis of 180 degrees and are apposed securely by a double ferrule at the end and by a tightening device over the handles, preparatory to placement of the anterior rows of sutures. One has, therefore, at his disposal two clamps held separately for the posterior suture and two clamps held rigidly as one instrument for the easier anterior suture.

Latterly a running suture of fine chromic gut (No 000) has been employed posteriorly as well as anteriorly in the row next to the clamps. After withdrawal of the clamps the anterior and posterior chromic gut sutures are tied to each other at both ends of the anastomosis. As before a row of Halsted mattress sutures of fine silk (DeKastel D test strength 25 pounds) is employed in the first posterior and the last anterior row. The finding of an occasional silk stitch dangling from the gastrojejunal anastomosis a few months after the operation by the gastroscopist persuaded me to make this trial. However at the same time the running suture approximation near the clamp reduces the time necessary for performing the anastomosis materially. This method of procedure has been eminently satisfactory and will prove probably more practical than anastomosis by interrupted sutures alone. I have had no occasion to doubt that a satisfactory mucosal approximation could be achieved by this method of anastomosis. An experimental study to appraise the mode of mucosal healing after gastrojejunal anastomosis with reference to the time factor in both open and closed anastomosis would appear to be worthwhile.

In side-to-side anastomoses, the portion of the viscus engaged above the clamp is not cut off with the cautery until the posterior sutures have been placed. The surgical diathermy is employed only on the stomach, 2 to 3 seconds (stop watch) of a moderately strong coagulating current sufficing to insure satisfactory

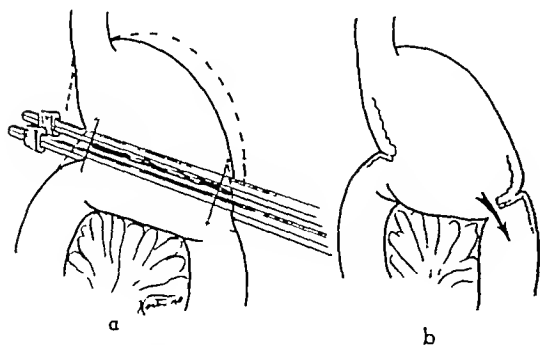


Fig 1 My conception of the usual cause of obstruction at the efferent outlet after gastrojejunal anastomosis (antiperistaltic) in the Hofmeister plan of gastric resection a, The surgeon should be careful to place his sutures in the jejunal wall at the  $\lambda$  mark. If he takes more of the readily available jejunum than he should (as shown in the triangulated area), of necessity considerably more tissue will be inverted than the surgeon intended, with ensuing narrowing of the efferent outlet. In the Hofmeister plan of procedure (antiperistaltic), on the afferent side, narrowing of the inlet does not accompany this oversuturing because inverted gastric wall is approximated to the triangulated jejunal wall without compromise of the stoma b, The effect on the efferent side is obvious. In addition to the consideration just described, it is important to place the sutures near the clamp. It is my plan to place the first posterior row less than 1 centimeter from the clamp. If this plan is adhered to rigidly, no more tissue will be inverted by the closed method than in the open anastomosis.

hemostasis. A metric rule is employed invariably to determine the exact lengths of the segments engaged in the clamps for the anastomosis to obtain absolute parity in length. The gastrojejunal anastomoses have been 6 centimeters and lateral anastomoses in the small or large intestine have been between 4 and 5 centimeters in length. A preliminary crush of the wall, prior to placement of the thin, narrow-bladed aseptic anastomosis clamp is employed only in the stomach, where great vascularity demands painstaking hemostasis. The large gastric crusher employed initially has been replaced by the clamps shown in Figure 8. The technique of gastrojejunal anastomosis by the closed method has been described in some detail at an earlier date (24). This paper proposes to deal essentially with the experiences gained in its use and the results obtained by closed anastomoses.

#### THE CLINICAL MATERIAL

For the purposes of this study, I propose to relate the experiences gained in 100 con-

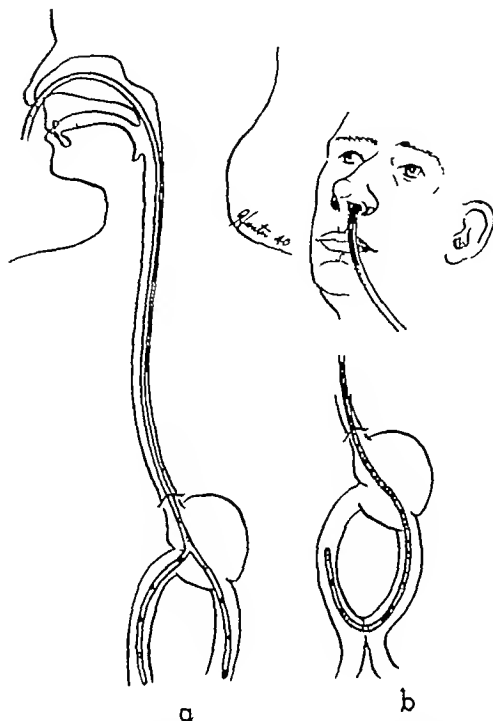


Fig 2 a, Use of the forked catheter to avoid distention of the afferent loop after gastrojejunal anastomosis. The 2 forks are tied together at the tip and the tube may be passed through the nostril without difficulty into the stomach. When operating for gastrojejunal ulcer, I attach an extra segment of catheter to the proximal fork and place it proximal to the oblique end-to-end jejunal anastomosis necessitated by detachment of the gastrojejunostomy. b, Use of a straight catheter for the same purpose when entero-anastomosis is made. Avoidance of distention of the proximal jejunal loop is probably an important item in gastric resection.

secutive anastomoses which I made in the alimentary canal, embracing a period of about 7 months since March 1, 1940. The larger number of operations to be reported concern the stomach, resection being done for ulcer in 48 patients and for gastric neoplasm in 35 cases. In 14 patients, colonic resection was performed, with re-establishment of intestinal continuity. In a miscellaneous group of 3 patients, a variety of operations were performed on the small intestine.

#### GASTRIC RESECTION BY THE CLOSED METHOD

The chief deterrent to earlier employment and acceptance of the closed anastomosis in the stomach has been probably on two scores. The first is the alleged danger of hemorrhage

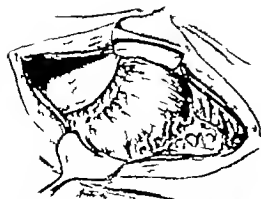


Fig. 3 The exposure through left subcostal incision. Ready access is had to the fundic portion of the stomach. duodenum may readily be dealt with through same incision.

Crushing of the gastric wall at the site chosen for the anastomosis, coupled with employment of the coagulating current of the surgical diathermy apparatus, has served to insure adequate hemostasis. In this group of more than 80 gastric resections there was only one instance of postoperative hemorrhage, occurring late in the convalescence. The residual stomach (resected for massive hemorrhage believed to be due to gastric ulcer but proved to be caused by carcinoma) and the stoma were negative on gastroscopic examination and the source of the bleeding was never determined. The patient has remained well. Employment of the Hofmeister plan of anastomosis, with oversewing and inversion of the oral or upper fragment of the divided gastric wall, beyond the 6 centimeters of the lower gastric margin needed for the gastrojejunal anastomosis, dispenses with the most vascular segment from which hemorrhage is likely to occur. Visible vessels on the external surface of the stomach in juxtaposition to the anastomosis are under run with a fine needle and ligated.

The other factor which may have deterred some from acceptance of the closed gastrojejunal anastomosis is fear lest failure to approximate the mucosa of the stomach and jejunum may be followed by untoward effects. It is to be admitted freely that a somewhat greater width of tissue is inverted by the closed method than by the open anastomosis. Yet the approximation must be very similar to that achieved by the Connell suture which

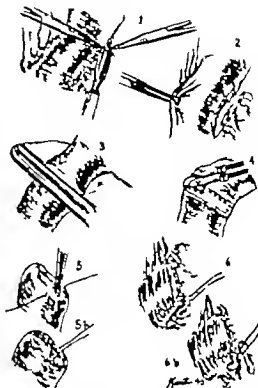


Fig. 4 The steps in direction and closure of the duodenum. Employment of the half purse strings at the ends combined with few ligated mattress sutures constitutes an eminently satisfactory method of closing the duodenum. The re-attachment of the pancreatic capsule (6 and 6b) affords assurance that secure closure has been obtained. (Reproduced from *Surgery* 640, 8 175.)

has been in use for 40 years in the open anastomosis. As related above a study of the healing process in open and closed gastrojejunal anastomosis upon the experimental animal would undoubtedly supply useful information. It would appear significant, however that gastrojejunal anastomoses with a 6 centimeter stoma with or without enteroanastomosis, function apparently quite satisfactorily. No patient operated upon by the closed method has had to be reoperated upon because of obstruction to the efferent loop.

Obstruction of the efferent loop has not been observed during our experience with gastric resection, with or without enteroanastomosis. However, as one patient, M. H. J., (see page 260) has shown, partial vomiting developed some months after operation. The pyloric portion of the gastroduodenal junction was done with end-to-side union between pylorus and stomach. An obstruction was found, but a flap of mucous membrane on the pyloric side appeared to be responsible for the pyloric obstruction. The patient has remained well. (See 1 for explanation of cause of this type of obstruction.)

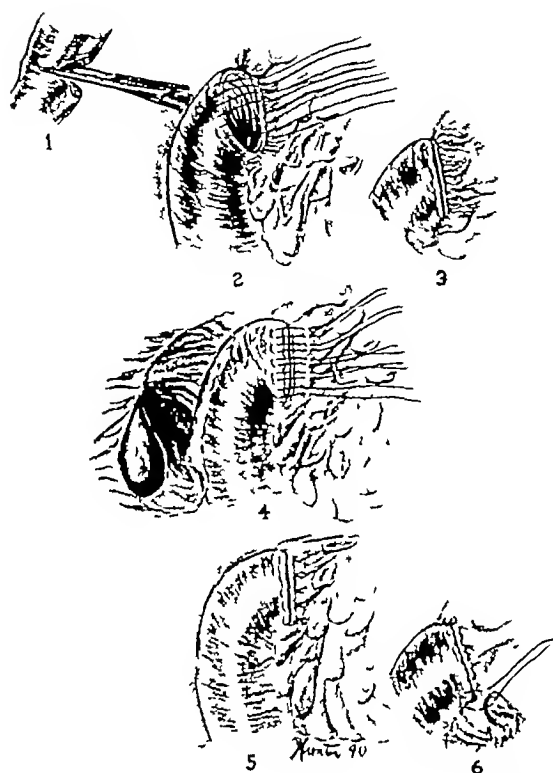


Fig 5 The steps employed in securing satisfactory closure of the duodenum in the presence of active massive hemorrhage from a duodenal ulcer and in nonbleeding cases in which there is a posterior wall duodenal perforation. Division of the avascular ligament of the duodenum, as shown in Figure 4, brings the duodenum nearer the midline and obviates tension. This separation permits also visualization of the common bile duct (4) and affords the surgeon reliable information concerning the extent to which he may mobilize the duodenum.

#### A LIKELY CAUSE OF OBSTRUCTION TO THE EFFERENT OUTLET

There is a point in the anatomy of a gastrojejunal anastomosis, especially after a high gastric resection, that the surgeon will do well to contemplate. This situation is depicted in Figure 1. It is to be noted that the width of the gastric wall may be the greatest at the clamp, while the walls of the small intestine, to be approximated to the stomach, slope away from the clamp, both above and below. In the Hofmeister plan a width of not more than 4 or 5 centimeters of gastric wall may be available for the anastomosis in high gastric resections, demanding sacrifice of 85 to 95 per

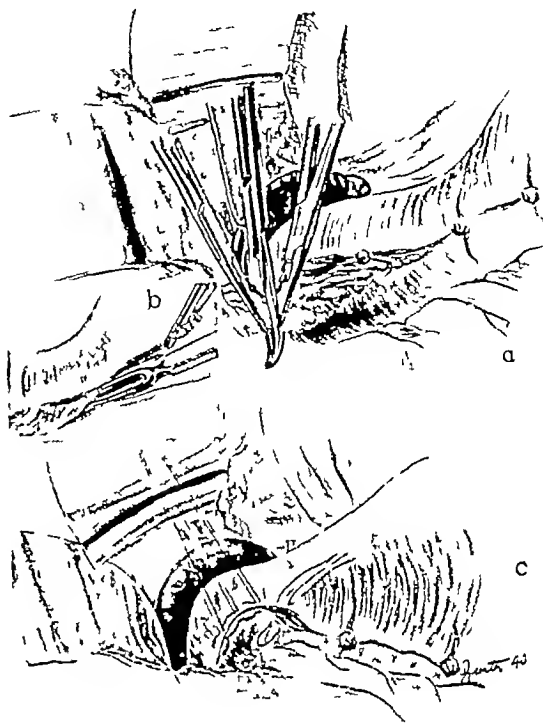


Fig 6 Preparation of the lesser curvature. a, Ligature of the left gastric artery. b, Division of the peritoneal folds (anterior and posterior) to the esophagus. c, Closure of the peritoneal defect at the upper end of the lesser curvature by interrupted silk sutures.

cent of the stomach in juxta-esophageal lesions which may be either ulcer or carcinoma. This means that unless the surgeon is wary, he may engage less of the gastric wall and more of the intestinal wall than he had in mind. In consequence, the efferent outlet, in antiperistaltic anastomoses made according to the Billroth II plan of operation, with such disparities in the lengths of the approximated segments will exhibit often definite narrowing. Through this agency, obstruction is less likely to occur at the afferent inlet in the Hofmeister antiperistaltic plan of operation, because inverted gastric wall is available for approximation without narrowing of the stoma. In my opinion, obstruction to the efferent loop, no matter whether the anastomosis is open or closed, is occasioned probably more often by the factor here described than by any other. The surgeon who employs the closed method tests always the patency of the stoma at the afferent

inlet and the efferent outlet. He knows when he has narrowed the gastric outlet. He knows too that a 9 centimeter anastomosis is no better than one 6 centimeters in length, if the efferent outlet is narrow. The surgeon who employs the open anastomosis assumes usually that the orifices of the stoma are patulous and terminates examination of his handiwork often by describing a "stoma admitting three or four fingers." The length of this opening is of no significance what really matters is, how large are the orifices of the stoma?

#### DANGER OF OBSTRUCTION TO AFFERENT INLET AFTER GASTROJEJUNAL ANASTOMOSIS

Whereas there are scores of papers in the surgical literature concerning obstruction of

the gastric outlet after gastric resection or gastrojejunostomy, there is scarcely any mention of the hazards of obstruction of the afferent loop. A few authors admit having observed gangrene of the retroperitoneal duodenum or the jejunum proximal to the anastomosis.

One of the best risks in the group of patients with carcinoma of the stomach died (M. S. S. L. No. 69583 aged 59 years) about 48 hours after operation with hyperthermia, the rectal temperature reaching 36 degrees Fahrenheit. Because of signs of cerebral irritation (positive Babinski and rigidity) it was believed that the patient died of cerebral accident. Permission for a autopsy was denied, but permission was granted to open the incision. The loop of jejunum proximal to the stoma was found rather dilated as was the retroperitoneal duodenum. The gut was not sectioned.

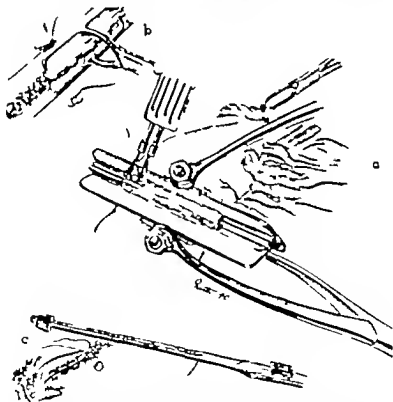


Fig. 7. Amputation of the stomach. a, Division of the stomach on the reaction ledge of the lower clamp (Fig. 8). b, Closure of the upper end of the amputated stomach. The clamp engages 6 centimeters of gastric wall for the anastomosis. c, The large gastric clamp has been removed and the aseptic reaction clamp has been pulled in the crushed groove. The area sutured over at the upper end is inverted with single row of interrupted mattress sutures of fine silk. The upper suture lies usually at the junction with the esophagus.

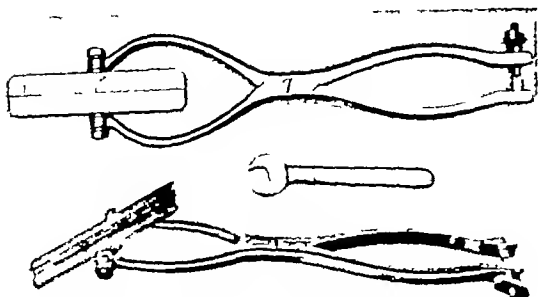


Fig 8 Gastric clamps for the closed gastric resection. The clamp above the wrench is applied first. By loosening the burrs above and beneath the blade, the handles may be rotated into the most convenient position. The clamp below the wrench presents a resection ledge. This clamp comes away with the segment of the stomach to be removed. Figure 7 indicates how the clamps are used in the closed gastric resection.

An entero enterostomy had been made at operation and 600 cubic centimeters of a bile stained fluid had been obtained with the intlying gastric tube in the first 24 hour period after operation. The next day 1250 cubic centimeters were obtained. The oral intake during the first 24 hour period after operation was 250 cubic centimeters and 800 cubic centimeters the second day.

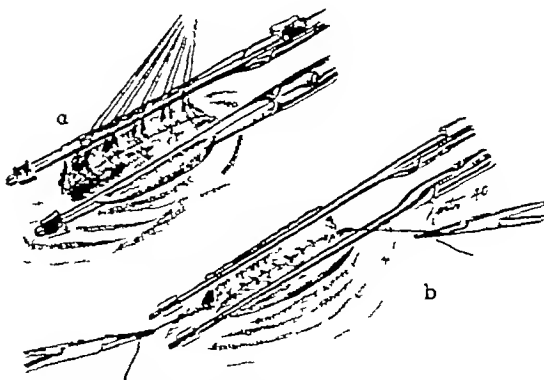


Fig 9 The posterior portion of the gastrojejunal anastomosis. a, Placement of the first posterior row of interrupted Halsted mattress sutures. These sutures are to be placed a distance of less than 1 centimeter away from clamp. (See caption, Fig 1.) Note position of the clamps, rotated to permit easy placement of the sutures. Five sutures are placed before any are tied. Four additional sutures are then placed between, making a total of 9 (usual number for a 6 centimeter gastrojejunal anastomosis). As each is tied, the assistant (second) who holds the clamps rotates them inward to afford maximal approximation at the site of tie. b, Second posterior suture (running chromic catgut No 000). Portion of jejunum above clamp not yet removed.

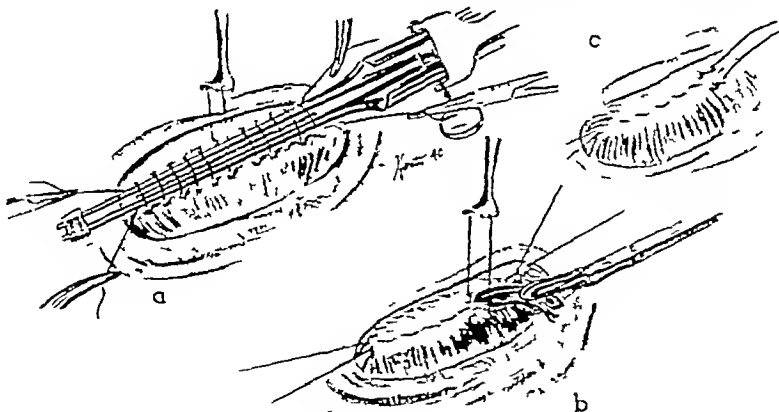


Fig 10 The anterior portion of the anastomosis. a, The jejunum above the clamp (Fig 9) has been cut away with the cautery—not directly on the clamp, but about 2 millimeters above the clamp. The single ferrules shown in Figure 9 have been removed, the handles of the clamps have been rotated, the double ferrule has been applied, engaging the tips of both clamps and the approximation device over the handles is in place. b, The running catgut suture shown in a is pulled upon after removal of the clamps. Elevation of the mid portion of the suture on an eyelid retractor permits aspiration of the residual gastric pouch with a sucker, after which the forked catheter is pulled out with an alligator type of forceps. A fork of the catheter is placed carefully into each jejunal limb of the anastomosis. c, After the forks of the catheter are in place, the anterior catgut suture at each end is tied to the posterior running catgut suture. Before these ends are tied, a fine silk suture is placed at each end, to prevent buckling or a "purse string effect" when the anterior and posterior sutures are tied.



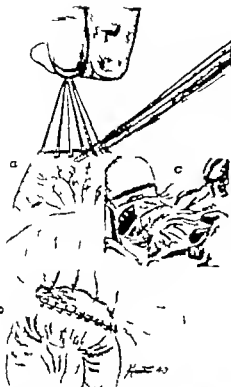


Fig. 2. a, Method of removing clamps in the anterior portion of the anastomosis. The tips of the clamps are depressed. The interrupted silk suture is shown here. b, The completed anastomosis below the transverse mesocolon. A single row of interrupted Halsted mattress sutures of fine silk completes the anastomosis. Three or 4 sutures serve to anchor the mesocolon to the gastric aff. anchoring sutures are placed in the jejunum. The residual gastric pouch seen from above the mesocolon.

On two occasions, at an earlier date, this same situation had been observed without obvious gangrene of the bowel. Both patients were exceedingly poor risks because of long standing obstruction. One of the patients had also a far advanced tuberculosis. Inasmuch as the histologic sections from the retro-peritoneal duodenum or jejunum proximal to the stoma failed in both instances to show any evidence of tissue change the local distention was explained away as being "paralytic" in origin. The surgeon was exonerated from blame and the cause of death was ascribed to the general debility of the patient.

In the instance of the patient referred to above however the stigma of protracted pre-operative obstruction was absent. It appeared

that slight rotation of the proximal afferent loop high on the lesser curvature may have kinked the bowel the entero-anastomosis constituting the only source for the escape of the duodenal contents into the stomach. Muddled of the observations of C. A. Dragstedt and his associates with reference to the effect of relatively low intraluminal pressures upon preventing the return flow of blood from the duodenum it was reasoned that the most likely cause of death in the patient referred to above was a closed-loop duodenal obstruction.

Together with my colleagues Drs. Lyle Hay and David Lynn a somewhat similar situation was established in dogs by dividing the pylorus and obstructing the jejunum a short distance beyond the duodenojejunal angle. Death from hyperthermia was almost a uniform finding. The intraluminal pressure in the obstructed duodenum was found to vary between 20 and 45 centimeters of water pressure in the dogs.

These observations will be reported in greater detail at a later date. Suffice it here to say that since the occurrence referred to above took place I have used a forked catheter with a tube in both the ascending and descending limbs of the anastomosis, without entero-anastomosis (Fig. 2). When entero-anastomosis is employed in carcinoma (but I am omitting it regularly now since using the forked intlying duodenal tube) the catheter is pulled down the efferent loop through the entero-anastomosis by means of a long alligator type of forceps with a blunt nose and the tip of the tube is placed well into the ascending limb of the stoma. I have now used the forked catheter without entero-anastomosis in a large number of gastric resections, including several virtual subtotal excisions for juxta-esophageal lesions in which 85 to 95 per cent of the stomach has been sacrificed. It is possible that mere placement of a straight tube through the gastrojejunal anastomosis into the proximal afferent loop would achieve the same purpose. Proper placement of a division of the forked catheter into the afferent loop is undoubtedly the more important consideration. Yet I feel a little more secure that the stoma will function satisfactorily on withdrawal of the tube 2 hours after operation.

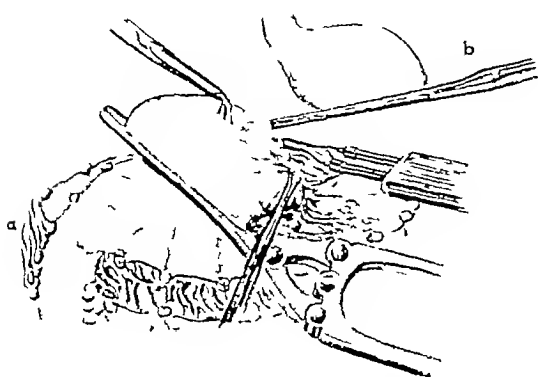
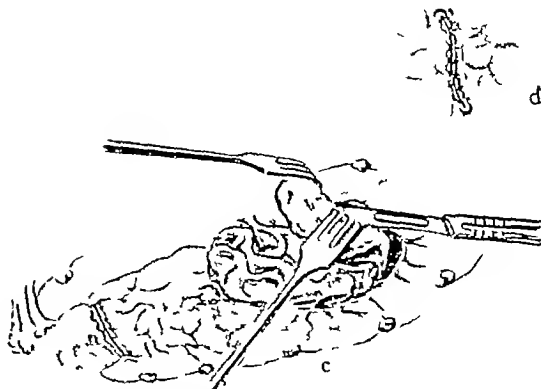


Fig 12 Method of dealing with a carcinoma of the stomach intimately adherent to the pancreas over a wide area a, The stomach is severed above the lesion After aspiration of the distal gastric pouch with a sucker, the posterior gastric wall is cut through with the cautery leav-



ing the adherent tumor on the pancreas b, The upper residual gastric pouch c, The residual tumor is shaved away together with a thin layer of pancreas d, Closure of the defect in the pancreas (transverse) with interrupted mattress sutures

when the forked tube has been in both afferent and efferent loops of the anastomosis

It appears somewhat strange that this factor of obstruction of the afferent loop should have received no discussion in the complications of gastrojejunal anastomoses I have the impression that it has loomed larger in the item of mortality after gastric resection than is apparent Patients who succumb from hyperthermia with "pneumonia or atelectasis" 36 to 72 hours after gastric resection should be examined critically with this consideration in mind Among the 4 deaths in the 100 consecutive cases reported herewith, pneumonia or atelectasis was not the primary cause of death in any instance

#### THE INDICATIONS FOR GASTRIC RESECTION

The two usual conditions for which one performs gastric resection are ulcer and neoplasm In the latter, sacrifice of a good portion of the stomach is obligatory if the tumor, whether carcinoma, lymphosarcoma, leiomyoma or polyp, is to be gotten rid of In ulcer, and especially in duodenal ulcer, gastric resection is an indirect attack on the ulcer diathesis, achieving its end by effectual reduction in gastric acidity, which attends regularly extensive resection and gastrojejunal anastomosis Gastrojejunostomy and other anastomotic procedures are not physiologic operations for ulcer, in that they fail to reduce

gastric acidity and leave too much to chance as evidenced by the high incidence of recurrent or stomal ulcers

#### PRE-OPERATIVE PREPARATION FOR GASTRIC RESECTION

There are certain fundamental requisites which must be met by all patients submitting themselves for major abdominal operative procedures They are especially mandatory in gastric surgery Patients must reach the operating table with the stomach empty This objective is achieved most readily by placement of an indwelling duodenal tube into the stomach to which suction is applied for an hour prior to operation, throughout the operative procedure, and for about 72 hours after operation In patients exhibiting high grade pyloric obstruction, a large gastric tube is employed for washing the stomach prior to insertion of the duodenal tube Even despite this ritual, in 3 or 4 of the carcinomas in this group, there was still considerable material left in the stomach at operation Vegetables eaten last by the patient a few weeks previously, in carcinomas with high grade obstruction have been removed through a gastrostomy opening at operation, immediately prior to undertaking the resection In large polypoid bleeding tumors, it may be necessary similarly to aspirate the intragastric hematoma resulting from manipulation of the stomach before

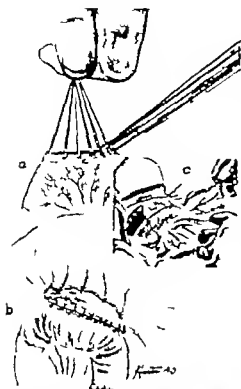


Fig. 1. a, Method of removing clamps in the anterior portion of the anastomosis. The tips of the clamps are depressed. The interrupted silk suture is shown here. b, The completed anastomosis below the transverse mesocolon. A single row of interrupted flaked catgut sutures of fine silk completes the anastomosis. Three or four sutures serve to anchor the mesocolon to the gastric wall. No anchoring sutures are placed in the jejunum. The residual gastric pouch seen from above the mesocolon.

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Fig 14 Gastric resection for posterior wall duodenal ulcer. a, The large dilated, obstructed stomach before operation. b, Residual gastric pouch after operation. c, The excised portion of the stomach (75 per cent). The ulcer is shown distal to the unrugated antrum. The rugations of the corpus and fundus are marked by contrast. The area of the excised specimen was 480 square centimeters (Type a resection as shown in Fig 13).



Fig 14c

a day in which 2 to 3 grams of sodium chloride is excreted. These are probably the most reliable tests of satisfactory hydration and chlorination. Occasional plasma chloride determinations serve as a satisfactory check against the development of hypochloremia. Careful weighing of patients immediately before operation and each morning for the early convalescent period after operation on a bedside scale helps to orient the staff in ascertaining the status of hydration of the patient (Fig 18). In patients with low cardiac reserve this expedient is most helpful after operation in determining the requirement of water.

Vitamins B<sub>1</sub>, C, and nicotinic acid are supplied in daily doses of 10, 50, and 100 milligrams hypodermically, respectively, for a few days prior to operation, and through a good portion of the postoperative period. Patients with both ulcer and carcinoma have observed

dietary restrictions usually and have taken, often in consequence, an inadequate amount of vitamins.

Anemic patients must be transfused with whole blood. In a few patients in this series, we were unable to get the hemoglobin above 50 per cent despite repeated transfusions because of persistent blood loss from an ulcerating carcinoma. Patients exhibiting shock from massive hemorrhage must have restoration of a contracted blood volume by transfusion before operation is undertaken.

#### SELECTION OF PATIENTS FOR OPERATION

*Ulcer.* In this clinic, the attitude of both internists and surgeons to the ulcer problem has been, in the main, one of great conservatism. A large number of patients presenting satisfactory indications for operation have, therefore, been accumulating in our outpatient

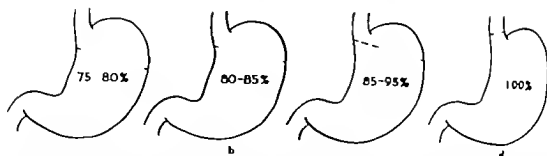


Fig. 3. Usual extent of excision of gastric tissue in the Hofmeister Pöly procedure: a, In ulcer, excision of 75 to 80 per cent of the stomach; with gastrojejunal anastomosis is necessary to insure achlorhydria; b, In carcinoma, even if the lesion is in the antrum, sacrifice of the entire lesser curvature is necessary to afford assurance that the disease

in the stomach has been eradicated. In juxta-esophageal lesions, no matter whether ulcer or carcinoma, subtotal sacrifice (85 to 95 per cent) of the stomach becomes necessary. The nature of the lesion present frequently has not definitely known until the lesion has been excised; d, Total gastrectomy.

the anastomosis is made. It is decidedly unsafe to leave the hematoma in the tiny residual gastric pouch, lest it be regurgitated into the trachea during recovery from the anesthetic. Keeping the stomach constantly empty during the induction of the anesthesia, throughout the operation, and during the early convalescence is the best assurance against pneumonia. Aspiration into the trachea is probably the most important cause of pneumonia in surgical patients. Pathologists have directed attention recently also to this occurrence.

The nutritional status of the patient should be satisfactory. In patients who are practically totally obstructed, this requirement may be extraordinarily difficult or impossible to meet fully. Yet, I have the impression that the necessity for the staged procedure—that is a preliminary jejunostomy or gastrojejunostomy—is largely a matter of past history. Unless a patient presents most unusual emaciation he can be prepared ordinarily for a one-stage gastric resection by para-oral feeding supplemented by white or fluid can be passed through the stenotic pylorus. No preliminary gastric drainage operations have been performed in this series of patients. None of the patients were refused gastric resection because of the presence of an obstruction in the pylorus.

The usual plan of procedure in obstructed cases is to supply nitrogen by giving human plasma in 500 to 600 cubic centimeter amounts, half the quantity being given twice

daily intravenously. This amount of protein will maintain the patient in satisfactory nitrogen equilibrium. My colleagues (26) and I have recorded in a preliminary communication elsewhere our experience with the intravenous administration of bovine plasma as a substitute for human blood or plasma in the treatment of contraction of protein stores or blood volume reductions. An enlarged experience suggests that this agency may come eventually to play an important rôle as a hospital procedure in the care of patients. The caloric requirement must be met by the slow intravenous administration of 10 per cent glucose solution (1000 to 1500 cubic centimeters). Not infrequently however feeding by a Murphy drip into the stomach of boiled milk to which lactose has been added (100 grams of lactose to 1 liter of milk) can be accomplished even though oral ingestion of 2 to 3 ounces at a time may be accompanied by vomiting or high grade retention. Another solution which affords a satisfactory means of supplying calories (carbohydrate) and protein is a mixture of 40 grams of casein and 200 grams of lactose in a liter of 0.45 saline solution.

Satisfactory water and salt balance are determined best by giving enough fluid to insure a urine output of 800 to 1000 cubic centimeters

Fertilized human eggs for intravenous use, which will maintain patients in satisfactory nitrogen equilibrium will come eventually to replace plasma for this same purpose. Recently we have been giving 100 cubic centimeters of 10 per cent glucose solution intravenously through a small needle placed in the small veins of the forearm. Surprisingly little serum flow (less than 100 cc) appears in the veins, but the fluid, given slowly (100 cc per hour) moves in some body during the long interval of administration.

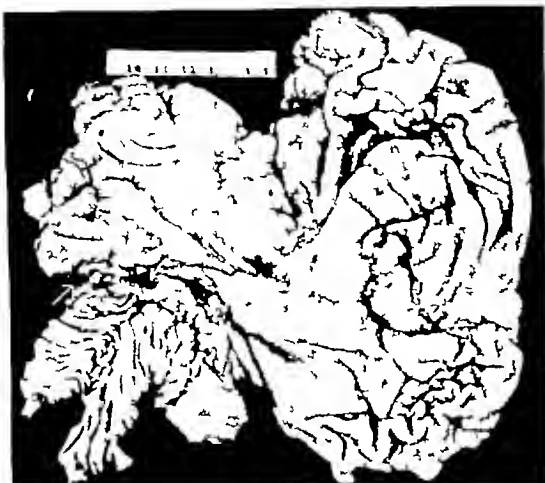


Fig 16 Emergency gastric resection for a bleeding gastrojejunal ulcer. The patient was 57 years of age and the gastrojejunostomy had been done 20 years before. Ten thousand cubic centimeters of blood was given prior to and during the operation. The operation was done in steep Trendelenburg position because of the difficulty in sustaining a stable blood pressure. The arrows indicate the ulcerations in the stoma. The area of the excised gastric tissue was 301 square centimeters.

gastric involvement and extensions unfavorable for an operative procedure commanding the risk of total gastrectomy. The 2 remaining patients exhibited carcinosis of the peritoneum and were rejected for even palliative partial resection. The resection rate in the patients explored for malignancy was 88.5 per

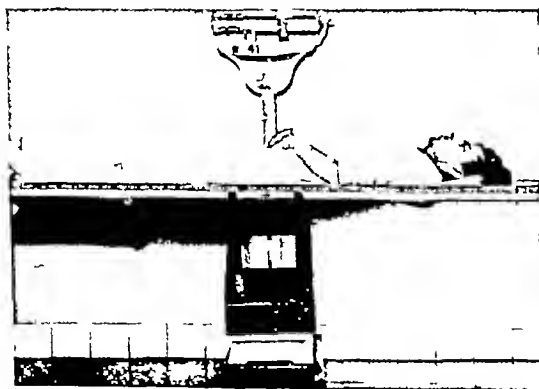


Fig 18 Manner of obtaining bedside weights of patients after operation. The block on the scale supports the stretcher. Significant gains or losses in weight may be detected readily. The weighing of patients before and after operation should come to be an important item in determining the status of hydration.

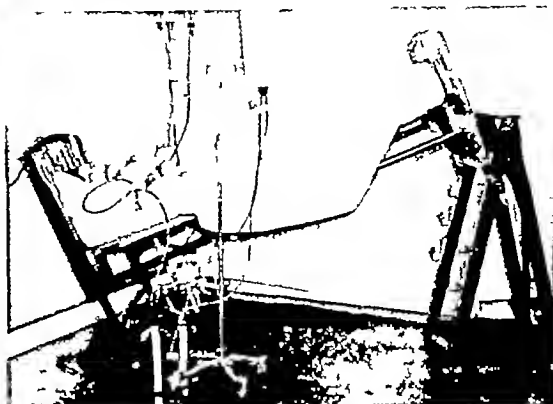


Fig 17 Shock frame employed routinely after major operative procedures performed under inhalation anesthesia. Placement of the patient in steep Trendelenburg position obviates aspiration of mucus or gastric content into the trachea while the patient is asleep. The naso-pharynx is kept dry by intermittent suction. The shock frame is of value also in supporting the blood pressure.

cent (31 out of 35 cases). No gastrojejunostomies were done for malignancy. The only gastrojejunostomy in this group of 100 patients was done for a patient with congenital cystic disease of the liver in which the liver cysts obstructed the pylorus.

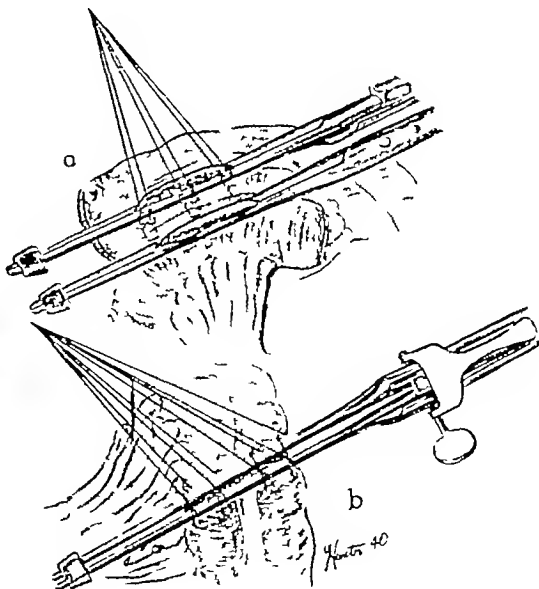


Fig 19 Closed anastomosis in the colon. a, Lateral anastomosis between the ileum and transverse colon after removal of a malignant tumor in the right half of the colon. b, Oblique end-to-end anastomosis in the pelvic colon.



Fig. 5c.

Fig. 5. Subtotal resection for *jucta-esophageal* lesion believed to be carcinoma, but found on microscopic examination to be *benign ulcer*. a, The large *jucta-esophageal* lesion on the lesser curvature. b, The large residual gastric pouch after sacrifice of 95 per cent of the stomach (Fig. 3 Type 1 resection). c, The excised stomach. The arrow indicates the site of the ulcer. The mucosal rugations are not prominent, even in the fundic position as contrasted with Figure 4. The stomach being considerably smaller than that shown in Figure 14 a, and even though 95 per cent of the stomach was sacrificed, the area of the excised specimen was only 307 square centimeters.

clinics for years. Of the 48 ulcers in this series, a fairly large number had had antecedent perforation or hemorrhage. Six patients (5 ulcers and 1 carcinoma) were operated upon during active massive hemorrhage. One boy of 14 admitted 5 times for acute massive hemorrhage was submitted to extensive gastric resection. Six patients in the group had gastrojejunal ulcer following an antecedent gastrojejunostomy. One of these had also a pyloric carcinoma and is placed therefore in the carcinoma group.

**Malignancy.** Obviously inoperable cases are turned away in the medical outpatient clinic. I am in no position to say therefore what proportion of patients in whom the

diagnosis of gastric malignancy was made came ultimately to gastric resection. Of the patients admitted to the surgical wards, all were explored but 1. This patient, though exhibiting an apparently operable lesion was found to have supraclavicular and pulmonary metastases. Six patients were explored but not resected. For 2 of these I had done an extensive gastric resection 4 years previously for carcinoma. On re-exploration, metastases were found in the liver. Another had a carcinoma involving both the lower esophagus and stomach and may not properly be considered, therefore to be a primary gastric neoplasm. Of the remaining 4 on whom exploration was carried out 2 exhibited total

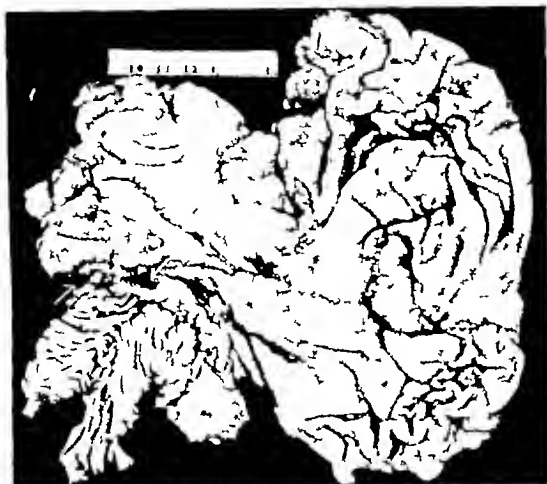


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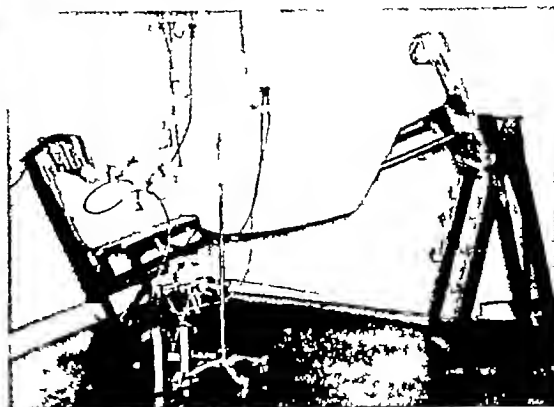


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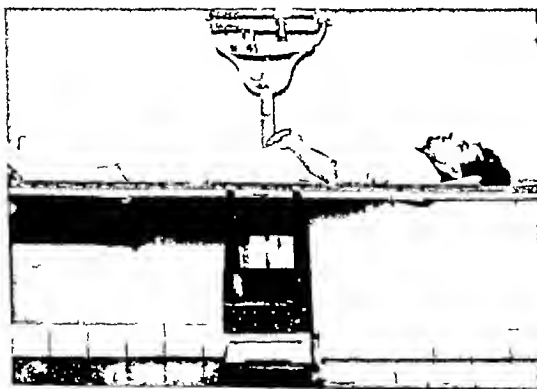


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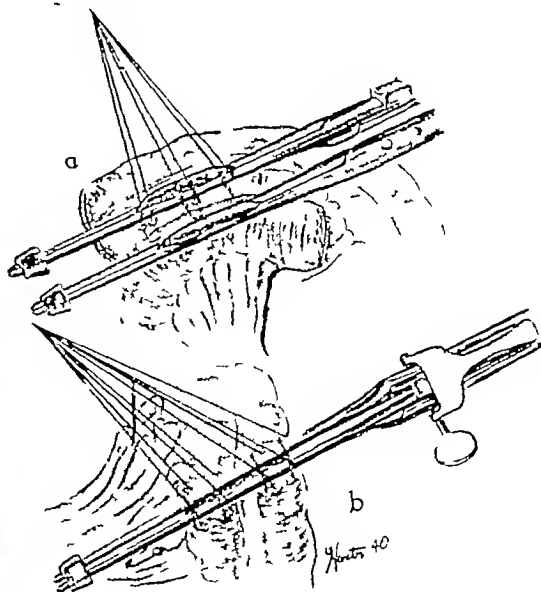


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b



Fig. 5c

Fig. 4. Subtotal resection for juxta esophageal lesion believed to be carcinoma, but found on microscopic examination to be benign ulcer. a, The large juxta-esophageal lesion on the lesser curvature. b, The tiny residual gastric pouch after sacrifice of 95 per cent of the stomach (Fig. 4, Type resection). c, The excised stomach. The arrow indicates the site of the ulcer. The pyloric projections are not prominent, even in the fundic position as contrasted with Figure 14. The stomach being considerably smaller than that shown in Figure 4 a, and even though 95 per cent of the stomach was sacrificed, the area of the excised specimen was only 297 square centimeters.

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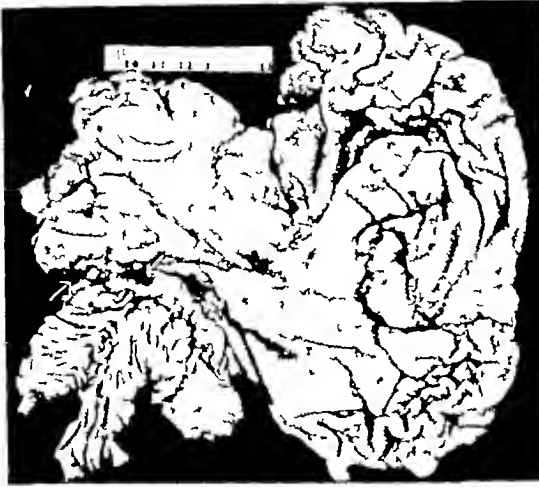


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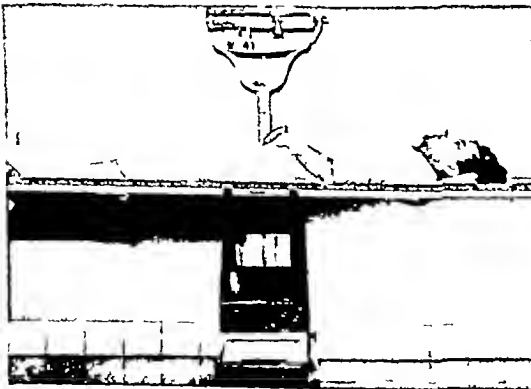


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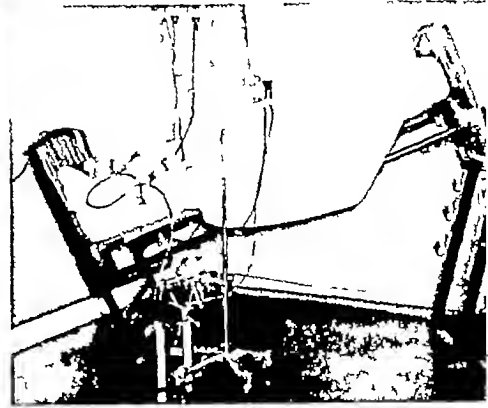


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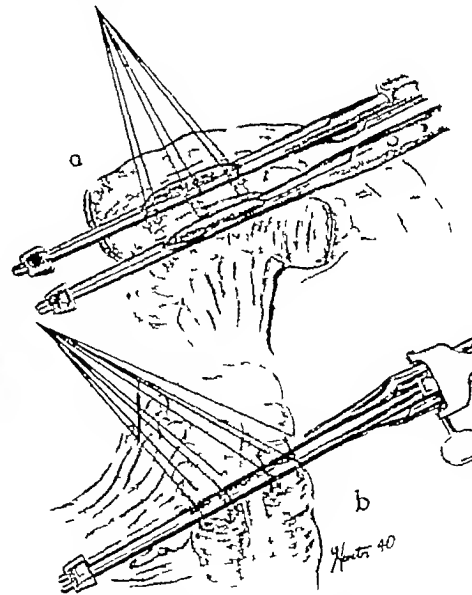


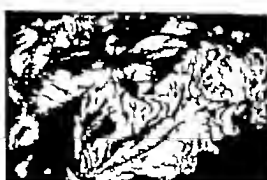
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Fig. 2a. High carcinoma of the cecum. a, left. A large necrotic ulcer is shown on the base of the cecum.



b, Perforation of the carcinoma onto an adjacent loop of small intestine.

Resection was carried out as a palliative measure in 2 patients exhibiting liver metastases. Adherence of the tumor to the pancreas or the transverse mesocolon was not considered as a contra-indication to operation, nor was extensive local lymph node involvement. In 1 case however an attempt to carry too far a difficult palliative resection in a man of 72 exhibiting a large periduodenal lymph node mass intimately adherent to the duodenal wall, eventuated in an insecure closure of the duodenum with resultant duodenal fistula from which the patient died 13 days after operation.

Nineteen or slightly more than half of the resection group for gastric neoplasm were over 60 years of age. Seven were 70 or over.

**Gastric polyps** In the medical clinic, all patients exhibiting gastric symptoms with negative x-ray findings are submitted to gastroscopic examination. Polyps are found not uncommonly in such patients. In the major ity we have awaited roentgenographic confirmation of their presence before submitting the patients to operation. There are 3 patients in this series, upon whom gastric resection was done for benign polyps. One of these was a man of 74 with jaundice from common duct obstruction. Four stones were removed from the common bile duct and the stomach was resected. The large gastric polyp which was believed to be malignant was found to be benign. The convalescence was uneventful.

#### THE OPERATION

All operations in the series were carried out under inhalation anesthesia. Cyclopropane

reinforced occasionally by ether was the anesthetic agent in all cases. All the gastric resections save those for massive hemorrhage were carried out through a left subcostal incision. An unusually satisfactory exposure of the entire lesser curvature and gastric fundus may be obtained through this incision. It is distinctly superior to a right or left rectus incision in affording access to the upper portion of the stomach. The character of the exposure obtained is indicated in Figure 3. At the same time the duodenum may be dealt with readily through the same incision. Its disadvantage as contrasted with the vertical incision is that it takes a little longer to make and still longer to close since the interrupted silk suture method is used. Evisceration has not as yet been observed with this type of incision.

#### TECHNIQUE OF GASTRIC RESECTION

The details of establishing the gastrojejunal anastomosis after gastric resection have been described previously. The variants in technique that have been adopted in the metamorphosis of the operation are not many and were alluded to briefly in an early part of this paper. The larger number of the gastric patients in the series, including all the neoplasms and the majority of the ulcers, were operated upon according to the Billroth II plan of operation, pylorus, antrum, and an extensive portion of the stomach being removed. In testinal continuity was obtained invariably by the Hofmeister plan of retrocolic, inferior terminolateral anastomosis (Fig. 7) Entero-

anastomosis was performed in all the carcinomas in the earlier part of the series and in a number of the resections for ulcer. With development of the forked catheter (Fig 2) to obviate stasis in the proximal jejunal loop, entero-anastomosis has been abandoned.

The greater omentum is excised regularly in gastric resection for malignancy. The pylorus and a good portion of the duodenal wall are then freed up by dissecting the medial or posterior duodenal wall free from the pancreas. The duodenum is divided with the Petz suturing apparatus, the crushed wall between the two rows of clips being cut with the cautery. The duodenum is inverted by the technique described previously. In 9 patients among the 48 ulcer resections, the duodenum was opened during the course of the dissection because of the presence of a posterior wall perforation. This is the invariable occurrence in operations undertaken during the course of active massive hemorrhage from a duodenal ulcer. The technique described previously constitutes a satisfactory means of closing the duodenum (25). I have had no experience with the pyloroplastic procedures described for dealing with this type of ulcer (Steinberg). As has previously been indicated, the consistent attainment of achlorhydria to histamine stimulation necessitates sacrifice of 75 to 80 per cent of the stomach. Because of the great tendency of gastric carcinoma to spread in the mucosa and submucosa (Verbrughen), I make it a regular practice, even in lesions limited to the antral zone, to excise practically the entire lesser curvature amputating the stomach from 1 to 2 centimeters distal to the esophagus on the lesser curvature. On the greater curvature, a greater length of gastric wall is left. Inasmuch as the only principal source of blood supply remaining to the small residual gastric segment, after this type of excision, comes from one or two of the vasa brevia of the splenic artery, it is very important to save the splenic artery, as well as these small branches. The usual upper sites of resection are indicated in Figure 13.

There was only 1 total gastric resection in the group. Only 2 have been done in the past year and both patients are well.<sup>1</sup> A number of

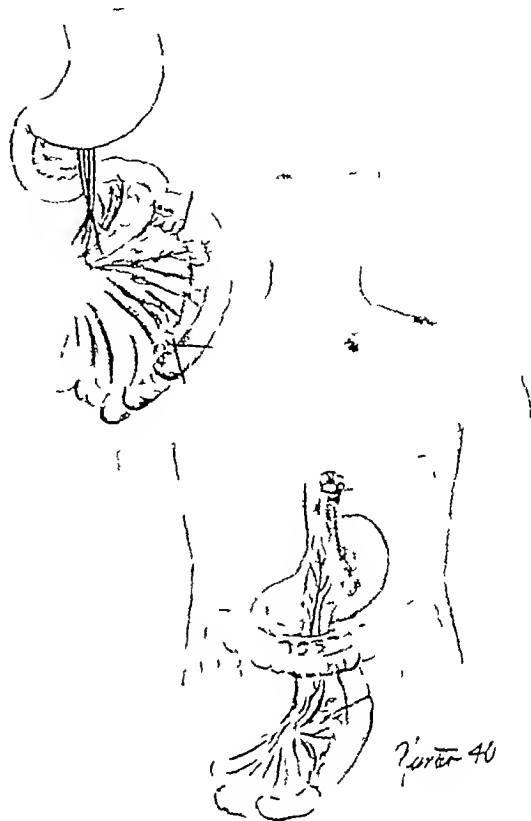


Fig 21. Schematic representation of gastrojejunoplasty (Wullstein Roux) as a feeding tube for carcinoma of the esophagus. A segment of the upper jejunum is isolated, the continuity of the small intestine being re established by oblique end to end anastomosis. An oblique end to side anastomosis is made between the aboral end of the isolated jejunal segment and the stomach. The oral end of the jejunum is brought out upon the thoracic wall to as high a level as the mesentery permits. Maintenance of the patient in a steep Trendelenburg position encourages migration of the small intestine to the upper abdomen and lessens tension upon the mesentery of the isolated jejunal loop.

virtual subtotal resections ranging from 85 to 95 per cent have been done, in which the lesser curvature was excised completely, either for juxta-esophageal ulcer or for carcinoma extending the entire length of the lesser curvature. The left subcostal incision and the Hofmeister plan of operation permit the anastomosis to be accomplished without difficulty. The success of the procedure depends in large measure on leaving at least one of the vasa brevia from the splenic artery intact.

<sup>1</sup>One additional total gastrectomy for leiomyosarcoma has been done since this paper was written. The patient did well.



Fig. 21. Gastric resection for Krukenberg tumor of the ovaries and uterus. *a*, left. The pelvic metastases excised at the first operation. The abdomen as the size of 6 months' pregnancy (see text). The excised stomach, excised 195 grams. It is to be noted the scale of projection is only one-half of *b*, *b*. The excised stomach, showing the superficial carcinomatous ulcer on the lesser curvature. Microscopic study of the stomach demonstrated that the tumor had spread widely in the mucosa and submucosa. The upper area of gastric resection as beyond the microscopic spread of the tumor however.

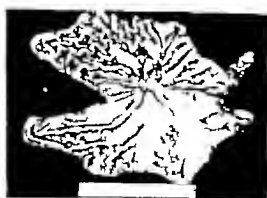


Fig. 22. The excised stomach, excised 195 grams. It is to be noted the scale of projection is only one-half of *b*, *b*. The excised stomach, showing the superficial carcinomatous ulcer on the lesser curvature. Microscopic study of the stomach demonstrated that the tumor had spread widely in the mucosa and submucosa. The upper area of gastric resection as beyond the microscopic spread of the tumor however.

For several months I have been employing the type of clamp depicted in Figure 8 instead of the usual Poirer or the large gastric crusher employed initially. The virtue of these clamps lies in this, that the clamp can be applied from the right side. After it is fixed in place the handles may be rotated by loosening the nut on the upper and lower blades. The likelihood of tearing the few remaining gastric vessels near the spleen is considerably less than with the use of the straight clamp. Further this new clamp<sup>1</sup> is especially adaptable for use in the left subcostal incision.

The illustrations made for me by Mr. Herbert Hunter indicate nicely the various steps in the procedure (Figs. 3 to 12). A special clamp 6 centimeters in length (Fig. 7b) insures engagement of the proper length of tissues for the gastroyejunal anastomosis. The method of dealing with the forked catheter is shown in Figures 1 and 10b. On completion of the anastomosis, the defect in the transverse mesocolon is closed by placing three sutures in the anterior gastric wall, about 1 centimeter behind the suture line. The incision in the abdominal wall is closed with interrupted sutures of fine silk. No drainage is instituted.

<sup>1</sup>The clamps and forked gastric catheter may be obtained through V. C. Mueller Company, Chicago, Illinois.

#### POSTOPERATIVE CARE

**Position.** The patient is maintained in moderately steep Trendelenburg position during the recovery period until he is fully awake (Fig. 17). Great care is observed to make certain that the indwelling tube is keeping the stomach empty. The nasopharynx and trachea are kept free from mucus by frequent aspiration with an electric suction apparatus until the patient is fully awake. After the patient is fully awake he may take sips of water by mouth, and the elevation of the foot of the bed on the shock frame is decreased gradually. Slight elevation of the foot of the bed is maintained, however well into convalescence, until the patient becomes quite active. Resumption of a steep grade of the Trendelenburg position is employed only for drops in arterial blood pressure.

**Vigorous movement of the extremities** is enjoined upon the patient from the very first day after operation. Nurses, internes, house officers, and staff admonish the patient to move his arms and legs a thousand times a day. I have the feeling that use of the Trendelenburg position and active motion are important items in thwarting pulmonary embolism.

**Fluid administration.** The fluid requirements of surgical patients have been very well

defined by Collier and Maddock and their associates. The careful notation and daily summary of the fluid administered, its amount and character, the fluid aspirated from the stomach, the amount of the urine and its sodium chloride content on the face sheets of the temperature record constitute a guide of the greatest importance in helping to orient the surgeon in the fluid and electrolyte balance of the patient. In a straightforward case, 3000 to 4500 cubic centimeters of fluid is given postoperatively each day for the first 2 or 3 days—sufficient to insure a urine output of about 700 cubic centimeters daily. Of this amount 500 to 1000 cubic centimeters is normal saline solution (4.5 to 9 grams of sodium chloride). The profound effect of prolonged operation and anesthesia upon the loss of fluid through the skin by sweating must be taken into account in the giving of fluid. Despite apparently generous administration of fluid, a lag in urinary excretion not uncommonly follows operation for a few days. As a matter of fact, some of our patients excrete only 300 to 500 cubic centimeters of urine of low specific gravity daily for the first 2 days. The ordinary surgical risk may be given fluid liberally (4500 to 5000 cubic centimeters daily) to increase the output of urine in the early postoperative period, but, as will be pointed out presently, this may prove a hazardous procedure in patients who are poor risks. Inspection of records indicate that 25 to 35 grams is the usual intake of sodium chloride as saline solution during the convalescent period. Many surgeons give far too much salt and invite pulmonary and general tissue edema in consequence.

We have erred occasionally on the other side and have not given enough sodium chloride to replace adequately that lost by sweating and that aspirated from the stomach (sodium chloride value of sweat estimated at 3 grams per liter and 5 grams per liter for gastric aspirations). The deficiency is suggested when the excretion of sodium chloride falls to less than a gram per day. Occasionally it is heralded by somnolence without obvious cause. It is startling to note how the administration of sodium chloride brightens and awakens such patients out of their drowsy

lethargy. An occasional plasma chloride determination serves to orient the staff correctly in appraising such situations.

#### BEDSIDE WEIGHING OF PATIENTS AFTER OPERATION

In old and feeble patients with impaired cardiac reserve, the orientation value afforded by frequent determination of the patient's weight cannot be overemphasized as a useful guide in determining the state of hydration. Weighing of the patient at the bedside will come to be undoubtedly a routine measure in ascertaining the fluid requirements of poor risk patients, whose margin of latitude for the tolerance of increases of plasma and extracellular fluid volume is very small. I have come to feel that the bedside weighing of such patients is an indispensable measure (Fig. 18). As a matter of fact, it is a good plan to ascertain pre-operatively the weight of all patients prior to major surgery. The loss of water by vaporization is so variable a factor that only the weighing scale can be depended upon for orientation in the patient whose capillary permeability, cardiac or renal reserve border on decompensation.

The lag in urinary excretion following operation is a variable factor. When a fairly liberal quantity of fluid has been given post-operatively and oliguria (daily urinary excretions of only 200 to 350 cubic centimeters) persists, it may be extremely hazardous to attempt to provoke diuresis by giving larger quantities of fluid by vein or under the skin. This lag in urine excretion is an interesting and perplexing phenomenon and deserves the serious attention of surgeons.

Weighing within 100 grams of absolute accuracy may be achieved readily. The confusion in the surgeon's mind with reference to the status of hydration in poor risks does not concern grams but weight disparities of 2 to 5 kilograms and more. Only he who has made these observations knows how disoriented he may become in reference to the status of hydration of his patient. Most of these errors concern the overadministration of water to patients with poor cardiac function. The heart may be well compensated before operation, but with the increase of plasma and



extracellular fluid volume which attends the too liberal administration of water compensation breaks.<sup>1</sup>

Inasmuch as a large number of these patients are in the upper age brackets and a number present evidence of cardiac damage, we have reverted largely to the subcutaneous administration of fluid. Intravenous administration of fluid accelerates the heart rate not uncommonly and now and then a patient complains of pain over his heart if the fluid goes in too rapidly. Blood plasma, and high concentration of glucose (10 or 30 per cent) must, of course be given intravenously.

**Shock.** The best treatment for shock is avoidance of blood loss. The operation is carried out in slight Trendelenburg position, the plane of the feet being a few inches higher than the head. This measure helps to support a stable blood pressure. A solution of 5 per cent glucose in distilled water is given subcutaneously during the operation quantities of 1000 to 1500 cubic centimeters being absorbed during the course of a 3 to 4 hour operation. A small needle is placed in one of the ankle veins through which saline solution, not exceeding 500 cubic centimeters in amount, is given. If the blood pressure tends to fall or the pulse accelerates, a transfusion of 500 cubic centimeters of citrated blood, or more if necessary is given. The shock frame shown in Figure 17 is an important item in supporting the blood pressure after operation. On return of the patient to the ward the nurse in attendance checks the blood pressure frequently during the early convalescent hours.

**The bladder.** So large a percentage of patients cannot void after these operations that I have come to insert an indwelling urethral catheter as a matter of routine. This practice helps also in determining accurately the daily urine output during the early convalescence. The subcutaneous administration of 1 to 2 grams of sulfanilamide avoids the occurrence of pyelonephritis.

**The siling duodenal tube.** Suction is kept up continuously until the forked catheter is removed 72 hours after operation. The pa-

1. In patient weighing 50 kilograms, postoperative weight gain of kilograms represents 100 cent of the body weight, but per cent of the body water (water constituting 65 per cent of body weight) it is obvious, therefore, that postoperative gain in weight must be watched in the post op patient with scrupulous care.

tient takes water and other clear fluids by mouth as soon as awake. After the tube is removed, the diet is increased gradually but patients are offered fluid and semisolid food in small amounts throughout the day until they can cough without pain. After that (about the sixth day) there is little likelihood of regurgitation of food into the trachea. When the patients leave the hospital they are instructed to take a well balanced diet. Ulcer patients are urged to eat meat again and they welcome the opportunity. Inasmuch as achlorhydria is the objective of the surgeon when operating for ulcer no dietary restrictions need be imposed on these patients.

**Pneumonia.** The incidence of pneumonia in this group has been surprisingly small, and the few pneumonias which were observed were largely benign. However it would be a serious omission did I fail to indicate the great protective value afforded by the intravenous use of sodium sulfathiazol or sodium sulfapyridine. Dr Wesley Spink of the medical service who has been keenly interested in the chemotherapy of surgical infections supervised kindly the treatment of the pneumonias. The usual dose of sodium sulfathiazol was 3 grams intravenously initially an additional gram or two being given every 4 to 6 hours. A daily dose of 6 to 8 grams was not exceeded.

In the older age group of patients (50 and over) I have come to substitute sodium sulfathiazol or sodium sulfapyridine for sulfanilamide in the prevention of urinary tract infection attending the temporary use of an indwelling catheter feeling that the drug may at the same time exercise a beneficial influence in thwarting pneumonia.

#### COLON RESECTIONS

The externalization operation of Bloch, Paul and Mikulicz constituted for years the preferred method of dealing with a large number of the malignancies in the colon. The relative safety of resection with primary anastomosis, whether in the right or left colon has come I believe to supplant largely the externalization operation. Complete excision of metastases in lymph nodes in the mesentery can be carried out far better with the primary resection and local recurrence is certainly less frequent than

with the exteriorization operation. My associate, Dr. Orwood Campbell, has for some time been an advocate of primary excision. Surgeons have been somewhat reluctant to give up the antecedent or complementary cecostomy or colostomy for left sided resections. In the earlier cases, I chose to establish, in unobstructed lesions of the left side, a simultaneous appendicostomy or cecostomy at the time of the resection. Latterly, following Campbell's example, I do not hesitate to perform resection of either the right or the left colon without a complemental external drainage vent. All patients, of course, have an indwelling duodenal tube, suction being maintained for 4 or 5 days. Whipple believes employment of the Miller-Abbott type of tube offers an important advantage and considers it to be, in his hands, an important factor in the reduction of mortality in primary resection of the colon. Our experience has been that suction, applied to an ordinary indwelling tube *from the beginning*, will preclude the occurrence of distention. In the 14 cases reported here, the only death occurred in a lesion in which perforation had occurred, occasioning contamination in the excision of the lesion.<sup>1</sup>

In acutely obstructed colonic malignancies, a preliminary drainage operation must of necessity be done. Not infrequently patients with mild obstructive symptoms may be tided over by a starvation regimen (clear fluids and suction applied to an indwelling duodenal tube) and operated upon as though obstruction were not present. With reference to acute obstructions of the colon with great distention, I feel it important to reiterate here the great value of the roentgenogram in ascertaining the point of obstruction and in determining the site to be selected for decompression. Cecostomy is to be avoided wherever possible, for it is not feasible to make readily an aseptic decompression on a very tense and distended cecum. On the contrary, decompression can be established in the transverse colon with ease and far greater safety to the patient.

In the colon resection group (14 patients) there were 10 right sided lesions and 4 left

sided lesions. Resection was performed in 1 instance in the presence of hepatic metastases. In 1 of the right sided lesions (perforated) a simultaneous partial excision of the circumference of the pelvic colon had to be made because of involvement by direct extension from the cecum. The continuity of the pelvic colon after the wedge excision was established by end-to-end suture. No external drainage vent was established. The operation was undertaken for supposed malignancy. The pathological diagnosis (gross) on the excised specimen was benign. The histologic diagnosis, however, confirmed the clinical impression of malignancy. Prior to operation, the mass had been believed to be outside the colon and the resection of right and left colon was done without preliminary cleansing of the colon. In the instance of a recurrent left sided lesion for which a previous excision had been undertaken elsewhere, the colostomy, which was involved by tumor, as well as the uterus was excised with primary establishment of intestinal continuity by end-to-end union. Two of the 14 patients exhibited benign lesions.

*Pre-operative preparation for resection.* The unobstructed patient is allowed only clear fluids by mouth for 3 days prior to operation. Three to 4 ounces of mineral oil are given daily during this time and the colon is washed out with liberal quantities of water twice daily. Nitrogen equilibrium is maintained by the intravenous administration of 500 cubic centimeters of human plasma daily. Caloric balance is approximated by the liberal administration of glucose solutions to supplement the oral intake. The water and salt balance are followed carefully even pre-operatively, as outlined above under the preparation of gastric cases for operation. I have had no experience with pre-operative peritoneal vaccination. The experience of this clinic suggests that, in the absence of a perforated lesion, a well performed closed anastomosis is the best protection against peritonitis.

*Anastomosis.* Partial colectomies are done through a vertical, right or left rectus incision depending on the location of the lesion, or through an oblique incision crossing the midline either above or below the umbilicus. In

<sup>1</sup>Four additional primary colonic resections have been done since the time of this report without mortality.

the right colon, side-to-side anastomosis between the ileum and the transverse colon is carried out usually (Fig. 19a). Occasionally,<sup>1</sup> an oblique end-to-side anastomosis is done. Ordinarily 2 to 3 feet of the terminal ileum are sacrificed with the cecum, ascending colon, hepatic flexure, and proximal transverse colon, making possible a more liberal excision of the lymph drainage area. Further the terminal few feet of the ileum exhibit often a narrower lumen than more proximal reaches. For lesions in the transverse splenic, descending, and pelvic portions of the colon, an oblique end-to-end anastomosis is made (Fig. 19b).

**Postoperative care.** This parallels in every way that of the gastric cases. The only important difference is that the inflying duodenal tube is kept *in situ* for 4 to 5 days. No enemata are given. The patient is allowed mineral oil by mouth 2 days after the indwelling duodenal tube comes out.

#### MISCELLANEOUS RESECTIONS

There were 3 cases in this group (1) a gastrotjejunostomy for congenital cystic disease of the liver (2) a jejunogastroplasty for carcinoma of the esophagus (3) a duodeno-jejunosotomy in a patient of 76 for obstruction in the retroperitoneal duodenum occasioned by a fixed irremovable carcinoma. All the patients recovered. In addition, there were 6 oblique end-to-end anastomoses in the jejunum, described as a part of the operative procedure in gastric resection for gastrotjejunal ulcer.

Only one of the procedures listed above is sufficiently interesting to merit special mention namely jejunogastroplasty for esophageal carcinoma. The procedure is not difficult to perform and the jejunum serves as a satisfactory tube for feeding. What is of most importance with reference to the problem of ultimate reconstruction of the esophagus, is that the oral end of the jejunum can be placed ordinarily well above the xiphoid process near the nipple line. Further final union between a skin tube and the jejunum can be achieved more readily than with the stomach. An oblique end-to-side anastomosis is made be-

<sup>1</sup>Lecturer in right sided ileum. They have making oblique end-to-end anastomosis between the duodenum and the colon. It is the simplest procedure.

TABLE I.—DIVISION OF MATERIAL AND HOSPITAL MORTALITY

		Number of cases	Operated deaths	Cases of recovery	Per cent mortality
I Gastric resections					
A Ulcer	43	8	80	6	
B Neoplasms	24		25		
Carcinoma	20		21		
Gastrocarcinoma					
Lymphosarcoma					
Polyps					
II Colon resections		12			
III Miscellaneous resections				3	
<b>Total</b>		<b>79</b>	<b>4</b>	<b>95</b>	<b>4.9</b>

\*During the period of time there were additional primary carcinomas of the stomach and colon (see text), which resections may not count. The resection rate for the gastric malignancies, therefore, 80 per cent (32 out of 33 cases). Jejunogastroplasty for feeding was done in the same 33 cases, but not resected. There was no surgical mortality.

Two final old lesions, among the very last to be operated upon, this series of 500 closed resections, but, since death, and the mortality for the series is, therefore, per cent and per cent, as stated, the table. One of these, Mrs. A. B. Carr, Group A, 1944-45, very little record of 71 operated on for carcinoma of the stomach, died on the 4th day of hospitalization from postoperative complications and heart failure. The other patient, Mrs. L. T. Carr, Group A, 1944-45, aged 72, was operated upon for (gastrointestinal) lesions, referred to be carcinoma, but which proved to be benign ulcer. Her immediate convalescence was satisfactory. Death occurred on day 2 after operation from massive (late arterial and venous thrombosis of a loop of terminal ileum). This latter case is the only mortality in the benign ulcer group. Hence the cause of this report is additional 23 primary gastric resections have been done for ulcer without mortality, including 4 benign gastric ulcers, gastropyloric ulcers, and gastropyloric ulcer lesions.

tween the aboral end of the jejunum and the stomach and intestinal continuity is established by an oblique end-to-end anastomosis. In all, 5 such jejunogastroplasties have been made (3 prior to and 2 since this series) without hospital mortality.

#### MORTALITY

The immediate results of operation on the 50 consecutive patients with closed anastomoses are shown in the accompanying tables. There were 4 deaths. Among the gastric resection group (83 cases) there were 3 deaths (3.6 per cent). In 48 benign ulcers, including duodenal, gastric, para-esophageal (4) and gastrotjejunal (5) there were no deaths. There was 1 death among 14 colon resections and none in a group of 3 patients with miscellaneous types of anastomoses.

#### OBSERVATIONS

It is to be observed that 3 of the 4 deaths were due to surgical blunders. The 1 avoidable deaths in the gastric malignancy group were due to technical errors: the 1 to obstruct

<sup>1</sup>See footnote accompanying Table I.

TABLE II—ANALYSIS OF CAUSE OF DEATH IN FATAL CASES

Date of operation	Name age and sex	Univ Hosp No	Diagnosis	Survival period	Cause of death	
					Unavoidable	Avoidable
5-31-40	S. S. 59 yrs M	U H. 695813	Carcinoma stomach (favorable)	48 hours		Distention of proximal loop of gastrojejunal anastomosis
8-27-40	F. C. 52 yrs M	U H. 654633	Pyloric carcinoma and gastrojejunal ulcer (favorable)	6 days	Coronary thrombosis	
8-29-40	F. R. 72 yrs M	U H. 698763	Carcinoma stomach (unfavorable)	13 days		Duodenal fistula and peritonitis
9-25-40	C. K. 6 yrs M	U H. 699541	Perforated carcinoma of colon (unfavorable) Colon resection and excision of right kidney and ureter	6 days		Peritonitis anastomosis intact

tion to the afferent duodenojejunal loop in the gastrojejunal anastomosis, the other to an insecure closure of the duodenum. The problem of closing the open duodenum in the so-called irremovable duodenal ulcer, or in the duodenal ulcer with massive hemorrhage, constitutes the most difficult task that the surgeon is called upon to deal with in gastric resection. There were 9 instances of perforation of the posterior duodenal wall in the ulcer resection group, necessitating the type of closure illustrated in Figure 5. There were 2 additional cases in which sealed perforations were present in the anterior duodenal wall demanding sacrifice of a more liberal portion than usual of the anterior duodenal wall. Yet, there were no deaths among these patients. Whereas, the mortality in the gastric neoplasm group was 85 per cent, the mortality should have been, when the avoidable deaths are deducted, 28 per cent.

The death in the colon resection group occurred in a patient with an adherent lesion perforated onto the right ureter and the retroperitoneal duodenum. Autopsy showed the suture lines to be intact. Peritonitis occurred from the apparently minimal contamination (no visible spillage) attending dissection and manipulation of the perforated lesion. Had the initial dissection envisaged the plan of excising the kidney, instead of accepting finally its necessity, the area of perforation would have been excised rather than broken into.

This is a problem peculiar to colon resections apparently. In the gastric resection group for malignancy, several instances were dealt with in the manner illustrated in Fig-

ures 4, 5, and 12, with evident source for contamination, but without apparent increase of risk to the patient.

#### LOCAL USE OF SULFANILAMIDE

Implantation of sulfanilamide (4 grams) was made about the site of contamination in the colon case referred to above, but without obvious protective value. My associate, Dr. Richard L. Varco, following the lead of Jensen, Johnsrud, and Nelson (1939), has implanted sulfanilamide about complicated gastro-intestinal anastomoses in dogs with considerable lessening of the mortality of such operations. This suggestion has been carried over into the colon resection group and into those instances among the gastric resection group for malignancy in which frank breaks in the aseptic technique were demanded by the type of case illustrated in Figure 12.

Varco appears to have established for the dog, at least, that the local implantation of sulfanilamide about the anastomosis has real value. It is to be recalled, however, that dogs tolerate large doses of sulfanilamide without evincing evidence of liver damage. Further, dogs do not acetylate or inactivate a portion of the sulfanilamide administered as does man. Varco's studies suggest, as did Jensen's earlier work, that local implantation is superior to its para-oral administration.

This aspect of the problem in man deserves thorough study. A local bacteriostatic or bactericidal agent which would be absorbed slowly, exerting a prolonged local effect, which could be left in the peritoneal cavity at the time of operation would be a great boon to the surgeon in dealing with the sealed perforation.

in colon resections. My experience suggests that the surgeon may excise sealed perforated gastric malignancies without apparent increase in the surgical risk. In the colon group he must bend every effort to *excise unopened* the site of perforation. Should the surgeon open into a perforated lesion, placement of sulfanilamide (4 grams) on a gauze sponge wrapped carefully about the area, should be done at once. In the fatal colon resection in the group sulfanilamide was placed at the site of perforation and about the anastomosis on completion of the operation—about 2 hours after the break in the aseptic technique occurred.

In the colon resection group including the patient who died perforation of the colonic malignancy into an adjacent loop of small intestine was observed 3 times. Carcinoma of the transverse colon, adherent to the stomach (2 cases) may necessitate simultaneous excision of a portion of the gastric wall. In large gastric malignancies however invading the transverse colon (1 case in this series) gastric resection and excision of the involved portion of the transverse colon, with performance of colostomy were carried out at the first operation with secondary establishment of continuity in the large bowel.

#### REMOTE RESULTS

This communication is essentially technical in character and does not propose to deal with the remote results of operation. A few general comments bearing upon the choice of operative procedure however may not be out of place.

#### THE PALLIATIVE OPERATION

Excision of the primary lesion with liver metastases was done twice in the gastric malignancies in this series and once among the colon group. A number of other obviously palliative procedures were done in the gastric group in which resection was performed in the presence of metastatic lymph nodes which could not be removed, when nodules were present over the diaphragm or in the cul-de-sac. One case is of particular interest in this connection. A synopsis of the patient's history follows.

Mrs. C. H., University Hospital No. 699368 aged 38 years was admitted to the gynecologic service for a large abdominopelvic tumor the size of a 6 months pregnancy. The tumor (Fig. 22a) was excised by Dr. J. L. McKelvey professor of obstetrics and gynecology and Professor Robert Meyer pathological attaché to Dr. McKelvey's department, stated that despite the absence of gastric symptoms the adenocarcinoma transplanted onto the excised ovaries and uterus was a so-called Krukenberg tumor and had its origin undoubtedly in the stomach.

After recovery from the initial operation, x-ray examination of the stomach was carried out—a small lesion being found on the lesser curvature. Gastroscopic examination confirmed this observation, and 3 weeks after the first operation gastric resection was performed. A small lesion difficult to palpate but with few juxtapositional lymph nodes as found (Fig. b) Because of the obvious lack of serosal involvement, it was postulated that the lesion probably had spread widely in the submucosa and mucosa (Verbruggen) and that excision of the entire lesser curvature was necessary. The only distant metastasis made out was a small nodule in the right lobe of the liver. When it was uncovered by retraction of the right costal margin on completion of the operation for the implantation of a radium seed, it was ascertained to be hemangioma. The pelvis was entirely free from tumor.

Is palliative surgery of this variety justified? I do not know and do not defend the thesis though I am trying to probe its rationale. It is obvious that greater risks are accepted for such patients than in the ordinary case. I believe such obvious transgressions of the usual orthodox indications for operation can be justified only if the risks of the procedure are not far out of line with the hazards accepted by standard risks. It is obvious that in the ultimate analysis the surgeon cannot in such a group demonstrate the same accomplishment as in the select cases.

I must confess to a feeling of some disappointment in knowing that 2 of the palliative gastric resections are exhibiting already within 4 to 6 months of the time of resection definite evidence of progression of their disease. Yet, I am cheered on to continue these apparently aggressive operations by the occasional patient who survives a palliative resection done in the presence of remaining metastatic lymph nodes for years. I have observed survival for a year following excision of a portion of the retroperitoneal duodenum for a polypoid bleeding tumor when

metastases were present in the liver at the time of operation. Another patient survived primary excision of the colon 15 months under the same circumstances. One patient with obstruction of the small intestine from a carcinoma still survives 2 years and 6 months after a short circuiting operation. The local lesion was not excised because of large metastases in the liver. The patient continues to hold his 70 pound weight gain since operation. What mechanism has restrained the growth of the neoplasm? If we only knew and could imitate or augment the mechanism, the cancer problem would be nearer solution.

The remote results in malignancies, favorable for excision, in the stomach or colon need no defense. Our own experience (Bergh) corroborates the published opinion of a number of writers on this score.

#### DIFFICULTY OF DISTINGUISHING GASTRIC ULCER AND CARCINOMA

Earlier recognition is still an obviously important item to anyone who reviews critically his own material. In this connection, it probably should be said that too large a number of gastric cancers come to operation after they have been treated for too long periods of time as gastric ulcer. The inability to distinguish between ulcer and carcinoma in certain cases is only too well known. It would appear that surgical excision holds out less risk to such patients than the "wait and see" policy. In this series there were several cases in which the histologic diagnosis had to be awaited before the true nature of the lesion was known. In such doubtful cases, more often than not, the lesion turns out to be an ulcer, but there are in this small series, 6 cases that proved to be malignant when the preponderant pre-operative evidence favored a benign lesion.

The small juxta-esophageal lesion is a particular problem (Finsterer, Rieder, Walters). Of the 5 in this series 4 proved to be benign. A benign ulcer here in our experience may be accompanied by a low free gastric acidity. A malignant prepyloric ulcer, however, may exhibit high gastric acidity. Achlorhydria to histamine stimulation is still a very important adjunct to the clinical, x-ray, and gastroscopic diagnosis of gastric malignancy.

#### RESULTS OF RESECTION FOR ULCER

An opportunity to follow patients in the outpatient clinic who have undergone operation for ulcer is a very gratifying and reassuring experience. The question of what might be expected of gastric resection is beyond the limits of this discussion and has been dealt with, in part, elsewhere (27). The majority of the ulcers in the series reported here had resection of 75 to 80 per cent of the stomach, including pylorus and antrum, after the Billroth II plan of operation.

#### SUMMARY AND CONCLUSIONS

The closed or aseptic method of anastomosis is an eminently satisfactory procedure for accomplishing continuity after resection in any portion of the alimentary canal. The surgeon is still the most important factor in the operative mortality of resections. In the 4 deaths which occurred in this series of 100 patients, there was only 1 unavoidable death (coronary thrombosis). The planned operation with studied thought lent to every detail of the procedure pre-operatively is the most important factor in achieving a reasonable mortality. Good anesthesia, trained and alert associates, intent on avoiding the numerous pitfalls which may overtake the patient in the convalescent period, and a seasoned experience, all play significant rôles in keeping operative hazard at a minimum. The blunders of the surgeon during operation, whether of commission or omission are usually beyond recall and are irreparable. On the contrary, mistakes made in postoperative management are amenable often to adjustment or correction by timely recognition, permitting salvage of the situation.

There were 3 deaths in the entire gastric resection group (83 cases), a mortality of 3.6 per cent. In the ulcer group (48 cases), including duodenal, gastric, juxta-esophageal, and gastrojejunal, there were no deaths. For the gastric neoplasm group (35 cases), the mortality (3 cases) was 8.5 per cent. One death in 14 resections occurred in the colon cases (7.1 per cent). In the miscellaneous resections (3 cases) there were no deaths. The resection rate for gastric malignancy in this group was 88.5 per cent (31 out of 35 cases).

Resections for ulcer. It is believed should be achieved with a mortality of about 2 per cent (unavoidable mortality). In the malignant group (both stomach and colon) avoidable deaths, due to errors of the surgeon, can never be eliminated entirely, probably yet it should be possible to perform both gastric and colonic resections with a mortality of approximately 5 per cent (unavoidable deaths).

Obstruction of the afferent loop in gastrojejunal anastomosis, without gangrene, hitherto undescribed, is pointed out as a likely important factor in the cause of mortality after gastric resection. Death, through this agency may occur also after simple gastrojejunostomy in the presence of high grade pyloric obstruction. Death occurs about 48 hours after operation from hyperthermia. The condition may be reproduced experimentally in the dog. Placement of a forked-type of catheter to which suction is applied in the ascending and descending limbs of the anastomosis eliminates the hazard of distention to the proximal loop.

The principles of pre-operative and post-operative management in patients undergoing gastric or colonic resections are reviewed. In particular it is suggested that the bedside weighing scale be employed as a guide in ascertaining the status of hydration in poor risk patients. The loss of fluid by vaporization is so variable a factor that the urine output cannot be used safely as the gauge for the quantity of fluid to be given. The compensation of poor risk patients given fluid by the usual standards of administration may break. Only the weighing scale can tell in patients with low urine output whether the water has been vaporized or is collecting in the extracellular fluid spaces. The latter occurrence may threaten disaster in patients with poor cardiac reserve.

The aseptic anastomosis, it is believed, extends the range of operability in resections in the alimentary canal without increasing the hazards materially over those accepted by standard or select risks.

## REFERENCES

1. ALLEN, A. W. and WELCH, C. E. Malignant disease of the colon: factors influencing the operability, morbidity and mortality. *Am. J. Surg.* 1930, 45 7.
2. BRADY, G. S. Seminar discussion on carcinoma of the stomach. January 1930. Unpublished.
3. CAMPBELL, O. J. Surgery of carcinomas of the colon. *Minnesota Med.* 1940, 3 5.
4. COLLIER, F. A. and MANNING, W. G. Water and electrolyte balance. *Surg. Gynec. & Obst.* 1940, 70 140.
5. DAUGHTON, C. A., LAO, V. F., and MILLET, R. F. The relative effects of distention on different portions of the intestine. *Arch. Surg.* 1930, 3 2157.
6. FOSTERMAN, G. B. and BALFOUR, D. C. The Stomach and Duodenum. Philadelphia W. B. Saunders Co. 1935.
7. FRIEDBERG, H. Das cardiale Magengeschwür. *Wien. klin. Wochenschr.* 1930, 3 104.
8. FOM, T., and SCHNEIDER, E. Netz extirpation bei der Magenresektion gegen Karzinom. *Deutsche Ztschr. f. Chir.* 1913, 3 17.
9. HENRY, E. E. and ARTERBACH, C. W. Aspiration bronchopneumonia, its special reference to operation of stomach content. *J. Am. M. Ass.* 1940, 5 184.
10. JESSUP, N. K., JOHNSON, L. W., and NELSON, M. C. The local implantation of sulfadiazine in compound fractures, preliminary report. *Surgery* 1930, 6.
11. LEVITSKY, E. M. and PAGE, G. T. End Results in the Treatment of Gastric Cancer. An Analytical Study and Statistical Survey of Sixty Years of Surgical Treatment. New York Paul B. Hoeber Inc. 1930.
12. MANTON, K. H. and BURDET, G. E. Aseptic end-to-end anastomosis and method for making closed intestinal loop suitable for physiologic studies. *Arch. Surg.* 1931, 21 36.
13. PARKER, E. M. and KERR, H. Intestinal anastomosis without open incision by means of heating stitches. *Johns Hopkins Hosp. Bull.* 1908, 9 12.
14. POC, A. E. Re-establishment of the gastro-intestinal passage after gastric resection. *Surg. Gynec. & Obst.* 1940, 70 270.
15. RABIER, F. W. An aseptic method of intestinal anastomosis. *Surg. Gynec. & Obst.* 1931, 47 38.
16. RABIER, F. W. and GRUBER, A. S. Cancer of the Colon and Rectum. Its Diagnosis and Treatment. Springfield, Illinois C. C. Thomas, 1930.
17. REIDER, W. Chirurgical Behandlung des Karzinoms des Uterus ventriculi. *Arch. f. klin. Chir.* 1930, 96 640.
18. SCHNEIDER, M. E. The surgical treatment of gastroduodenal ulcerations: the technique of gastric resection. *Surg. Gynec. & Obst.* 1930, 7 57.
19. STONE, H. B. Method of intestinal anastomosis with new clamp. *Surg. Gynec. & Obst.* 1917, 65 145.
20. VASCO, R. L. and HA, L. J. The value of the local implantation of crystalline sulfadiazine about gastro-intestinal anastomosis in dogs: valuable adjunct in the prevention of peritonitis. *Surgery in press.*
21. VERMIGLIA, A. Intraluminal extension of gastric carcinoma. *Proc. Staff Meet. Mayo Clin.* 1933, 6 765 (University of Minnesota Master's Thesis).
22. WALTERS, W. Cardiac gastric ulcers. *Arch. Surg.* 1940, 4 542.
23. WALTERS, W. and CLEVELAND, W. H. The surgical treatment of gastric cancer: summarizing as benign disease. *Minnesota Med.* 1940, 3 709.

- 24 WANGENSTEIN, O H Aseptic gastric resection I A method of aseptic anastomosis adaptable to any segment of the alimentary canal (esophagus, stomach, small or large intestine) II Including preliminary description of subtotal excision of the acid secreting area for ulcer Surg, Gynec & Obst, 1940, 70 58
- 25 Idem The problem of surgical arrest of massive hemorrhage in duodenal ulcer the technique of closing the duodenum Surgery, 1940, 8 275
- 26 WANGENSTEIN, O H, HALL, H, KREMEN, A, and STRUTTS, B Intravenous administration of bovine and human plasma to man proof of utilization Proc Soc Exper Biol & Med 1940, 43 616
- 27 WANGENSTEIN, O H, VARCO, R L, HALL, L J, WILKINS, S, and TRACH, B Gastric acidity before and after operative procedure with special reference to the rôle of the pylorus and antrum a preliminary report of a clinical and experimental study Ann Surg, 1940 21 626
- 28 WHIPPIT, A O The use of the Miller Abbott tube in surgery of the large bowel Surgery, 1940 8 289
- 29 WILKINSON, D P D Cancer of the colon and its surgical treatment Lancet, 1934, 1 65



# THE SURGICAL TREATMENT OF GASTROJEJUNOCOLIC FISTULA

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THE most dreaded complication of gastro-enterostomy is the formation of a common fistulous communication between the stomach, jejunum, and colon due to the perforation of a stomal or jejunal ulcer into the adherent colon. Very seldom the lesion may result spontaneously from carcinoma of the stomach or colon which traps the adjacent hollow viscera and ulcerates through their walls. In any event the consequences of such a union are disastrous. Pain may be present but curiously enough, may disappear on formation of the fistula. Severe gastric indigestion occurs with belching of foul smelling gases and, at times, vomiting of material resembling colonic contents. Diarrhea is the rule and may be severe. Undigested particles of food may be noticed in the stool. Loss of weight begins at once and is often rapid and extreme. Anemia, avitaminosis, and senous fall in serum proteins develop and in severe diarrhea there may be dehydration and marked imbalance of chemical plasma structure. In a matter of months or even weeks, the patient's physical condition is reduced to a point which renders extremely dangerous any attempt to carry out the procedures necessary for ablation of the fistula and restoration of continuity. Furthermore all tissues adjacent to the fistula are often edematous, inflamed, and heavily infected in this manner increasing the operative difficulties and inviting postoperative complications.

That this picture is not overdrawn is shown by the mortality figures. No series, personal or collective, thus far reported has shown a mortality of less than 25 per cent and from this it has ranged up to 63 per cent in most skillful and experienced hands. I suspect that a complete collective study. If it could be made, would reveal the situation as even worse

since I have found that single sporadic cases in which operation was done in various clinics by methods hitherto employed have almost invariably resulted fatally and are not reported.

The chief causes of death are shock, peritonitis, pulmonary complications, leakage, usually from the repaired colon embolism and hemorrhage. Almost all patients coming to operation have already reached the stage of severe malnutrition, either because of failure to realize the rapid deterioration which follows formation of the fistula or because of prolonged ineffectual efforts to control it by medical management. There is no medical treatment for this condition other than the measures necessary for rehabilitation prior to surgical attempt at cure. On the other hand to operate precipitately without rehabilitation is almost equivalent to a death warrant.

The measures available are principally transfusions of whole blood and especially plasma, a high vitamin, high protein and caloric diet, and bed rest. Opium is of value in reducing intestinal irritability and, for diarrhea such agents as kaolin and bismuth are helpful. Alkalies are not always of value and may be harmful as tending to increase the danger of hypochloremia. By such means, carefully carried out, Collier (personal communication) reduced his mortality from about 40 per cent to approximately 12 per cent in simple reconstruction operations.

But not all patients can be rehabilitated so long as the fistula is actively conveying colonic contents into the stomach and jejunum. A plan is now presented by which this can be prevented, wherein in the vast majority of cases symptoms can be completely alleviated and rapid restoration of the patient effected to a state in which any radical procedure indicated to remove the fistula and also deal with the ulcer diathesis can be done with no higher

mortality than is inherent in the procedure itself

This plan requires the adoption of preliminary colostomy proximal to the fistula as a first stage. In May, 1938, I presented before the American Surgical Association observations on the value of preliminary colostomy in the correction of gastrojejunocolic fistula. This paper cited 3 cases of ultra-severe fistula, 2 of my own and 1 of Colp, who adopted the suggestion originally made in an earlier report of the first case. For the argument, reference should be made to the paper in the *Annals of Surgery*, October, 1939, but the experience gained pointed unmistakably to the conclusions drawn. In order to check those conclusions for the purposes of this communication, a letter was sent to each member of the American Surgical Association to ascertain how often the plan advocated had been employed, with a note of results and observations. The response was prompt and practically complete. No attempt was made to gather the entire experience of the membership with this lesion as it was believed that an adequate cross-section of results with other plans existed in the literature. The replies have brought the total of patients treated by preliminary colostomy followed by resection or restoration to 15. All were males who had had a previous gastro-enterostomy for ulcer with the single exception of Morton's case of spontaneous formation of this lesion due to a malignant tumor of the stomach. This patient was a female. Ten were treated in the second stage by gastric resection, 5 by simple restoration. Fourteen recovered, 1 died, a mortality of 6.6 per cent. A brief summary of the cases listed under the name of the contributor is as follows:

#### CASE REPORTS

CASE 1 (D B Pfeiffer) Male, aged 34 years, had had gastro-enterostomy for duodenal ulcer 4 years previously. The patient had improved until the onset of the present symptoms 5 months before admission. He complained of severe diarrhea, foul belching, and a voracious appetite. His weight loss had been 30 pounds. There was moderate anemia. The abdomen was boggy, slightly distended, and peristalsis hyperactive. At x-ray examination barium passed through the pylorus but mostly through the anastomosis and with incredible rapidity

through the small intestine. No barium could be seen passing directly from the stomach into the colon but by barium enema it was seen to enter the stomach at a point proximal to the splenic flexure. October 2, 1936, an exploratory operation was performed. The stomach, jejunum, and colon were found matted together, there was considerable free fluid. All the adjacent tissues were acutely inflamed and edematous. There were two separate jejunal ulcers distal to the anastomosis. Radical surgery was absolutely contra-indicated. An ascending loop colostomy was done and was opened on the third day. *All the symptoms disappeared at once.* After the contents of the distal colon had been expelled, there were no further bowel movements. The patient gained 50 pounds in 4 months. On February 1, 1937, operation was performed. Inflammatory changes were absent, there was no free fluid, the separate jejunal ulcers had healed. The original ulcer had apparently healed. The anastomosis was taken down without difficulty and repair of the stomach, jejunum, and colon carried out. There was marked distention following the operation. Because of the fear of leakage from pressure, a simple pursestring jejunostomy was done on the third day. Further convalescence was uneventful. The patient has remained well to the present time.

CASE 2 (D B Pfeiffer) Male, aged 39 years, had had an appendectomy in May, 1927. Simple suture for perforated duodenal ulcer had been performed in August, 1929. A recurrent duodenal perforation developed in February, 1937. Suture of the perforation and a posterior gastro-enterostomy were done. Following episodes of pain in the left lumbar region the patient had developed symptoms of a gastrojejunocolic fistula 1 month before admission to the hospital, June 3, 1938. His present symptoms included diarrhea, fecal vomiting, and belching of foul gas, diffuse abdominal pain, and a more than 10 pound weight loss in a month. There were present moderate anemia, epigastric tenderness, and hyperperistalsis. Roentgenographic examination showed the opaque medium leaving the stomach through both pylorus and anastomosis and from jejunum directly into colon. A barium enema showed prompt entrance of material from the transverse colon into the stomach and jejunum. On June 8, 1938, an exploratory operation was performed. The entire area of the anastomosis and transverse mesentery was found to be inflamed and edematous. A loop colostomy of the mobilized ascending colon through a muscle splitting incision in the flank was done and opened 5 days later. *All digestive symptoms disappeared.* Normal stools were obtained by colostomy, occasionally by rectum. The patient had a marked gain in weight and remained well. He was readmitted 4 months later for the second operation. The pylorus was patulous and the old ulcer apparently had healed. Inflammatory changes at the site of the fistula were entirely absent. Disconnection of the anastomosis and a fistula measuring 1 by 3 centimeters were disclosed. The defects were closed

A paucistruing jejunostomy was done recovery was uneventful. The spur was destroyed, the colostomy closed, and the patient discharged 5 weeks after his admission. His original duodenal ulcer has been reactivated and resection has been advised. On present opinion is that it would have been better judgment to have resorted at the second operation.

CASE 3 (Dr Ralph Colp.) Male, aged 49 years, had undergone posterior gastro-enterostomy for duodenal ulcer on January 7, 1935. Recovery was uneventful. There were no symptoms for 3 years. Three months before his second admission, April 3, 1938, the patient began to have diarrhea, belching of foul smelling gas, and a rapid loss of weight. A barium enema revealed a gastrojejunoileocolic fistula. An ascending loop colostomy was performed on January 9, 1938, and was opened on the sixth day. All symptoms disappeared. The patient gained 8 pounds in 3 months. A fistula could not be demonstrated by x-ray examination. Operation was performed on July 6, 1938. A hard inflammatory mass involving stomach, jejunum, and colon was disclosed. There was healed jejunal ulcer inches below stomach. The fistula had closed. A subtotal gastric resection was done by the Holmeister antecolic method. Repair of the colon and end-to-end union of the jejunum was carried out. There was moderate postoperative reaction, but the patient was well by March, 1939, and had gained 5 pounds.

CASE 4 (Dr J. H. Gibson, J.) Male, aged 38 years, had undergone posterior gastro-enterostomy for ulcer in 1924. The patient entered the Pennsylvania Hospital in March, 1939, with marked diarrhea of 6 weeks duration. His weight was 6 pounds there had been a loss of 15 pounds in 6 weeks. T. bacilli of the right upper lobe was present the sputum was positive. A barium enema showed rapid filling of the stomach from the colon. Reverse passage was not seen. Medical management for 8 weeks resulted in no diminution of diarrhea and a further weight loss of 5 pounds. On May 29, an ascending colostomy was done. Co valence was complicated by the appearance of a tender inflammatory mass in the left lower quadrant with fever which gradually subsided. The diarrhea continued but his weight remained stationary at 97 pounds. As a result of intensive intravenous therapy with blood and plasma transfusions, his weight picked up 15 pounds in 4 weeks although he continued to have one or two movements by rectum and lost considerable food by direct passage from the stomach through the fistula into the colon and by reverse peristalsis from the distal end of the colostomy. On August 1939, gastric resection with removal of the fistulous area in one mass was carried out with resection and anastomosis of both the jejunum and colon. Operative recovery was satisfactory. Two months later small intestinal obstruction from an adhesion in the pelvis was relieved by operation. At present, a year later the colostomy is closed and his general condition is excellent.

CASE 5 (Dr S. C. Harvey.) Male, aged 4 years, had had a posterior gastro-enterostomy in 1924. Moderate relief was obtained for years then massive hemorrhage developed. 1 October 1926, a pyloroplasty was done, restoration by Roux-Y. Relief was obtained only for 1 month. R. operation was done in 1929. The patient stated that no ulcer was found. Cholecystectomy for pericholecystic adhesions was done. Improvement was short, followed by ulcer symptoms and repeated tarry stools. He was admitted to New Haven Hospital in December 1930. Considerable relief was obtained by medical management but his symptoms recurred and an operation was done elsewhere for jejunal ulcer. Excision of the ulcer was carried out with resection of the old gastro-enterostomy and the making of a new one. His symptoms persisted, and the patient was readmitted to New Haven Hospital in July 1937. Again the patient improved on the Sippy regimen. He was readmitted 1 year later. Weeks previously he had begun to have severe diarrhea, passage of undigested food in the stool, rapid loss of 15 pounds in weight. A gastro-intestinal series revealed a gastrojejunoileocolic fistula. His general condition still remained reasonably good. On June 6, 1939, preliminary double barreled ileostomy was done. On June 30, 1939, the H. lineist type of gastric resection was carried out. Recovery was uneventful. An end-to-end anastomosis of the colon was done. The ileostomy was closed. September 6, 1939. On November 7, 1939, the patient was symptom free.

CASE 6 (Dr J. T. Priestley, M.D., Clinician.) Male, aged 48 years had had posterior gastro-enterostomy for ulcer in 1933. Temporary relief had been obtained. For the last 3 years, the patient had had severe diarrhea with passage of undigested food and loss in weight of 5 pounds. His serum protein was 3.7. On August 3, 1939, proximal transverse colostomy was done. Ascites as present all the tissues were edematous. General improvement resulted but leakage of gastric contents from the distal limb of the colostomy occurred until this was plugged. A transfusion was given on August 4, 1939. Serum protein was 5.9. A partial gastrectomy by the posterior Polya method and closure of the colon and jejunum were carried out. Convalescence was uneventful. On December 1939, the patient was well and had gained 35 pounds.

CASE 7 (Dr C. Mathewson, J.) Male aged 50 years, had undergone posterior gastro-enterostomy for ulcer in May 1920. The patient was well for years, then recurrence of the ulcer symptoms took place. Two months before his admission to San Francisco Hospital, severe diarrhea began with vomiting of foul material and rapid loss of 15 pounds in weight. A barium enema showed gastrojejunoileocolic fistula. Operation was performed on June 1936. The colon was detached and repaired, the jejunum repaired. The gastro-enterostomy was not taken down. Convalescence was stormy. The diarrhea stopped but ulcer symptoms persisted. On his re-

admission to the hospital, September, 1939, a gastrojejunocolic fistula again was present. There was further loss of weight (present weight 97 pounds, best weight 180 pounds). Hyperperistalsis was present. An operation was performed on October 10, 1939, an exteriorized cecostomy was done. *All the symptoms disappeared.* The patient gained 34 pounds in less than 2 months. A second operation was carried out on January 16, 1940. Inflammatory changes were absent. The colon was freed and closed. A fistula 3 centimeters in diameter was disclosed. A gastric resection by the posterior Polya method was performed. Recovery was uneventful. The patient has been well to date.

CASE 8 (Dr C Mathewson, Jr) Male, aged 39 years, had had a perforated duodenal ulcer in 1929. Closure of the ulcer and a posterior gastroenterostomy were carried out, but the ulcer symptoms persisted. In 1938 a marginal ulcer was diagnosed. The patient was readmitted January 31, 1940, with symptoms of a gastrojejunocolic fistula of 2 months' duration. Severe diarrhea was present, pain had disappeared but there was much belching of foul gas and some vomiting. A considerable loss of weight had occurred. Hyperperistalsis was present. A barium enema showed a gastrojejunocolic fistula, barium by mouth did not show it. Barium passed from the stomach to the colon in 30 minutes. On February 3, 1940, a loop transverse colostomy was made. *There was only one stool by rectum after the colostomy was opened.* There was a gain of 16½ pounds in weight in 5 weeks. Re operation was done on March 3, 1940. Inflammatory changes were absent. The colon was detached and repaired. A fistulous opening 5 centimeters in diameter was found. A posterior Polya resection was performed. Some wound infection developed. Otherwise recovery was uneventful. A barium enema later showed that the repaired colon had opened to some extent (had colon been functioning this would in all probability have caused death). Seven weeks later, however, the colon was closed with good recovery.

CASE 9 (Dr R R Graham) Male, aged 42 years, had had a posterior gastro enterostomy 3½ years previously for severe ulcer symptoms and repeated hemorrhages. Improvement took place for 6 months, then recurrence of the symptoms developed. Three weeks previously the patient had felt something give way in the abdomen followed by vomiting which became foul. Diarrhea which scalded the skin around the anus occurred. The pain ceased but the patient lost 20 pounds in 3 weeks. On September 9, 1939, an ascending loop colostomy was done. *All of the symptoms stopped.* The patient gained 18 pounds in 1 month. ("This man's progress following the colostomy was unbelievably delightful. After a week, one could wash the distal colon without any going into the stomach." R R G.) On October 25, 1939, re-operation was performed. A slight edema was still present about the area of the lesion but not of any moment. The colon was separated,

a fistula 1 by 1½ inches was found. The colon was repaired, and the jejunum transected and anastomosed. A subtotal gastric resection by anterior Polya method was performed. Convalescence was complicated by massive collapse of the left lung with some pneumonia but recovery was good. Fistula closure, 3 weeks later, was not entirely successful due to infection but was completed readily later. Recovery to date has been complete.

CASE 10 (Dr A W Allen) Male, aged 56 years, had had a gastro enterostomy 10 years previously. Diarrhea and typical symptoms of gastro jejunocolic fistula were present. The patient had lost 30 pounds. On September 14, 1939 a right colostomy was performed. The patient's general condition was much improved though the 3 pound weight gain was not impressive. On January 6, 1940, a subtotal gastrectomy was performed with transection and anastomosis of both the jejunum and colon. Prompt and uneventful recovery occurred. A gain of 27 pounds in 6 weeks took place. Colon has closed and patient is in excellent health.

CASE 11 (Dr H Trout) Male, aged 40 years, had been treated at Veterans Hospital, and the records are sketchy. Posterior gastro-enterostomy had been performed 4 to 5 years previously for ulcer. Symptoms of marginal ulcer had been present for about 18 months, foul breath, diarrhea, vomiting of fecal material for the past few months. Medical management gave no improvement. A gastrojejunocolic fistula was demonstrated. An exploration was done in August, 1939. The general condition of patient was wretched. He was little else than skin and bones. Local edema and inflammation were present around the lesion. An ascending loop colostomy was performed. ("I don't think I ever saw a patient's general condition improve more quickly." H T.) A second operation was done 5 to 6 months later. The patient's general and local condition were entirely satisfactory. Excision of the fistulous tract and restoration of continuity were effected. Recovery was uneventful. The patient was placed on ulcer regimen to prevent reactivation of the original ulcer but he has remained well and has gained 30 to 40 pounds in weight.

CASE 12 (Dr J J Westermann) Male, aged 42 years, had had a Roux type of gastro-enterostomy (no ulcer established) in 1934. In 1936, an exploration was carried out for a supposed marginal ulcer. The attempt was abandoned "because of adhesions." In 1938 (J J W) the gastro-enterostomy was undone, the ulcer was excised, an entero-anastomosis and high gastro-enterostomy were performed thus closing the previous stoma. In 1939, a jejunal ulcer developed 1 in below the stoma. The gastro-enterostomy was undone, the jejunum was repaired, pylorectomy and posterior Polya carried out. A subtotal resection was decided against because of the technical difficulties. The patient's symptoms reappeared and a gastrojejunocolic fistula occurred in January or February, 1940. In May, 1940, a transverse colostomy was performed. The pain

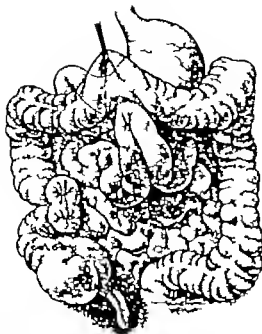


Fig. T. Stage operation for gastrosplenocolic fistula. Plicator (spondylagrammatic) exploration of lesions, ascending loop colostomy.

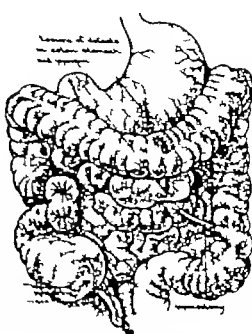


Fig. T. Stage simple restoration. With repair of defects in stomach, colon, and jejunum. Jejunostomy operation.

was relieved, appetite and nourishment improved, although there was loss of liquids through the colostomy. On July 9, 1910, re-operation was carried out. A subtotal gastric resection, a Pólya antecolic repair of the jejunum, resection of the colon and anastomosis, jejunostomy were done. Convalescence very smooth. I attribute the survival of this patient to the presence of the colostomy. (J J W.)

CASE 3 (Dr J J Morton.) Female, aged 53 years, complained of increasing epigastric pain, nausea, and vomiting for 6 months, eructations but no diarrhea, and a weight loss of 5 pounds. A barium enema showed rapid passage from splenic flexure of the colon to the stomach and jejunum. Barium meal showed a fistula from the post. wall of the stomach to the jejunum and colon. On May 5, 1910, an exploration was carried out. A large mass, the size of a large orange and thought to be carcinomatous, was revealed which involved the stomach and bowel but was otherwise free. A transverse colostomy following the Devine method was done. The patient's convalescence was reasonably uneventful. Fifteen days later the jejunum was freed and repaired. The gastrosplenic mass was excised. A subtotal gastrectomy was performed by the Hofmeister operation end-to-end union of the colon was carried out. Surprisingly comfortable convalescence. (J J M.)

CASE 14. (Dr J D Bigard.) Male, aged 48 years, as admitted to the hospital in July 1910. A

gastro-enterostomy had been done 8 years previously. Duodenal ulcer. H. had remained all for 7 years. His history indicated the development of jejunal ulcer years previously and gastro-jejuno-colic fistula 3 weeks previously. In that period he had had severe diarrhea and had lost 35 pounds. Fluid and chemical balance was secured and an externalizing cecostomy as performed. Prompt cessation of the diarrhea and gain of pounds in 3 weeks resulted. On August 7, 1910, the gastro-enterostomy was taken down, end-to-end aseptic anastomosis of the jejunum and of the colon was performed. The patient's convalescence was eventful.

CASE 5 (Dr F W Bancroft.) Male, had gastrosplenocolic fistula of some duration. General condition of patient was satisfactory. In May, 1910, an ascending colostomy by the Devine method was carried out. There was constant irritating discharge from the distal opening. The patient continued to lose weight and strength. In July 1910, because improvement seemed otherwise impossible, he was re-operated upon. A very large fistula, as found and difficult penetrating ulcer into pancreas. Subtotal resection was carried out. The patient died the ninth day after operation because of leaking duodenal stump with subperitoneal abscess. ("I would have done much better if I had done Devine type of pyloric exclusion instead of attempting to dissect the duodenum." F W B.)

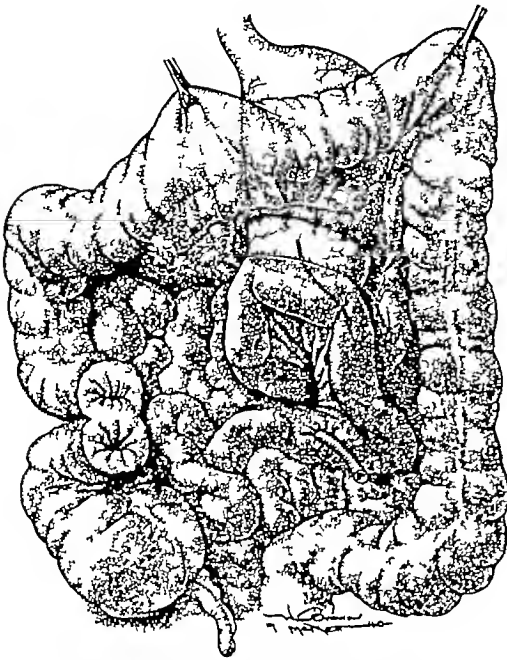


Fig 3 Second stage, second method (preferred), partial gastrectomy, excision of fistula, repair of jejunum, restoration of continuity (Pólya)

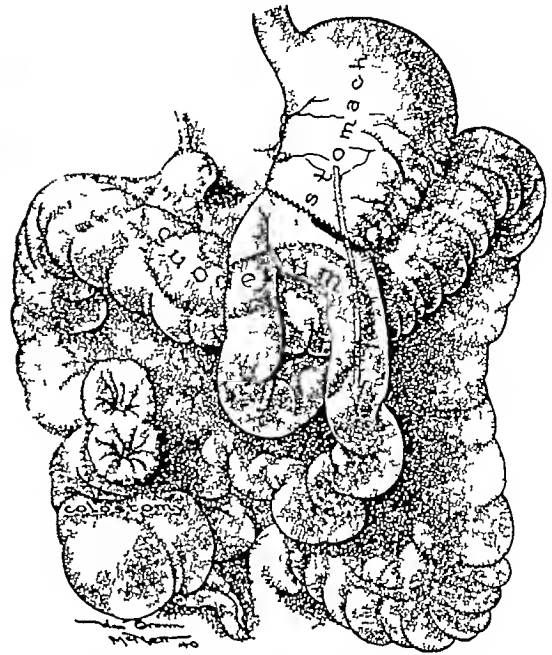


Fig 4 Preferred method Subtotal gastrectomy, antecolic gastrojejunostomy (Pólya or Hofmeister)

#### EVALUATION

It is now possible to re-examine the conclusions and recommendations originally made in the light of the findings in the present series of 15 cases. These additional cases represent the experience of a relatively small group of American surgeons with this plan in a period of only a little more than a year.

The important conclusions referred to were that (1) the loss of food from the stomach into the colon is ordinarily not significant, (2) the rapid weight loss and general deterioration of physical condition is not due to starvation from this food loss nor is the diarrhea caused by the entrance of gastric contents into the colon, (3) the important cause of serious symptoms is the continued entrance of colon contents into the upper gastro-intestinal tract, (4) loop colostomy proximal to the fistula abolishes symptoms, thus permitting rehabilitation to the point that adequate corrective surgery may safely be done upon the fistula.

When these statements are considered in order, it is found that no detailed information

as to food loss into the colon is available in 3 cases except that symptoms are said to have subsided after colostomy. In 3, however, it is stated that no bowel movements occurred after the colostomy, in 1 instance for as long as 4 months. Yet each of these patients had been having severe diarrhea with marked loss of weight. There was prompt gain of weight in each case. In 5 patients there was more or less loss into the colon but diarrhea ceased and weight gain was about as satisfactory as in those patients who showed no loss at all into the colon. The explanation of this curious observation is to be found in the fact that the entrance of colonic contents into the upper gastro-intestinal tract sets up irritation and violent hyperperistalsis. This is a common clinical observation and is confirmed by the roentgenologist. In my first case Stewart observed barium to pass in a rush from the upper jejunum to the lower ileum in 3 minutes. Mathewson has given me the notes of a case of fistula in a patient suffering also from active pulmonary tuberculosis upon whom he has performed the preliminary colostomy with

marked improvement in general condition and cessation of diarrhea. The second stage is being deferred for maximum improvement. The remarkable confirmatory observation in this case came about through the difficulty in maintaining the colostomy as a complete one. On two occasions the colostomy retracted and both times the re-entrance of colon contents into the distal loop caused diarrhea. On both occasions repair of the colostomy was followed by stoppage of diarrhea. Mathewson states (personal communication) that experimental work inspired by this observation confirms that the entrance of colonic contents into the jejunum causes diarrhea. This then may be the full explanation of the diarrhea and appearance of undigested material in the stools so often noted. In addition to the disturbance of nutrition due to hyperperistalsis, disturbed digestion, and absorption it is highly probable that the absorption of the toxic products present in the colon when introduced into the upper digestive tract must have a deleterious effect upon the general condition.

But it is necessary to state that in some cases there may be considerable loss directly into the colon. Priestley and Westermann each noted annoying loss of fluids from the proximal end of the colostomy but in the first instance it was stopped by plugging and in the second was not serious. In Gibbon's patient there was large and serious loss into the colon after colostomy with continuance of diarrhea and lack of the prompt and striking improvement almost uniformly noted. However this patient had active pulmonary tuberculosis. After the colostomy some sort of intra abdominal inflammatory complication occurred with formation of a mass in the left lower abdomen which gradually subsided. In spite of this, improvement was slowly brought about aided by intravenous vitamin treatment and he was able successfully to make a gastric resection. Note however that 2 months after this operation the patient had small intestinal obstruction requiring operation from which he recovered, and his present condition is excellent. It seems likely that the intra-abdominal complication after colostomy interfered with small intestinal function and caused the upper gastro-intestinal con-

tents to be shunted into the colon. The later occurrence of actual obstruction fortifies this assumption. The only fatal case in the series (Bancroft) also leaked freely from the colostomy and failed to get relief. Operation was done upon this patient in the belief that further rehabilitation could not be accomplished. The fistula was very large. Resection was difficult because of low lying duodenal ulcer. Death occurred as a result of leakage from the duodenal stump.

These observations enable us to restate our conclusions with slight modifications. It is clear that the typical diarrhea, loss of weight, and deterioration of general condition are commonly due not to gastric or jejunal loss into the colon but to the entrance of feces into the upper gastro-intestinal tract. It is strikingly demonstrated that these symptoms are ordinarily abolished at once by proximal loop colostomy. In a small minority of cases important loss into the colon may occur and may continue after colostomy. As to the cause of this phenomenon not enough data are available. It is not due to the size of the fistula alone. It occurs too seldom to vitiate the benefits of preliminary colostomy which has other advantages besides.

It is noteworthy that the only death in the series occurred in the only patient in whom rehabilitation could not be effected. This fortifies the opinion already stated that many patients cannot endure the necessary surgery while in their usual depleted condition. All pre-operative measures available should be employed before operation and this applies also to preliminary colostomy or jejunostomy performed in an attempt to improve the condition of an almost inoperable patient. Several such attempts have resulted fatally. Jejunostomy has occasionally helped but in general has failed to improve nutrition. It has no such striking effect as colostomy. The information received shows clearly that there are a considerable number of patients who cannot be rehabilitated so long as the colonic fistula continues to pour its products into the upper gastro-intestinal tract. Some cases reach a state in which even colostomy cannot be withstood. Muller, Allen, Golden, and McKittrick have sent the notes of such cases.

The operation of choice in these patients is subtotal gastric resection. This may be necessary because of conditions at the pylorus but even if the original ulcer seems to have healed experience shows that simple restoration of continuity is followed by reactivation of the ulcer in at least 20 to 25 per cent of the cases. Coller (personal communication) after an experience of 40 per cent mortality appreciated the necessity of rehabilitation by every measure before attempting cure by operation. After this regimen was instituted, 2 patients died, but since that time he has had a remarkable run of 16 operative recoveries with one stage operation. However, only 1 resection was performed. The remainder were simple restorations accompanied in 5 instances by pyloroplasty for stenosis of the pylorus. Already there have been two recurrences of duodenal ulcer. I do not deny that patients who are or can be brought in good general and local condition may be operated upon in one stage by the experienced surgeon with reasonable mortality. Allen's aseptic resection is technically of the highest order but it restores the patient to his ulcer diathesis as already mentioned.

A suggestion of merit in the one stage operation is to avoid the danger of leakage from the repaired or anastomosed colon by bringing the ends out of the incision for later closure in the Mikulicz manner. Both Lee and Joyce relate successful cases done by this plan. That leakage from the repaired or anastomosed colon is a chief danger is a well known surgical fact. It is also known that the best way to prevent such an accident is to defunctionate the colon. This is another advantage of the operation here recommended. There is then no risk in dropping the colon, because it is functionless. Mathewson in his second case actually found by x-ray a small leak which had produced no symptoms. Later, continuity was restored without incident. If a double-barreled colostomy is to be left for later closure, why omit the superior advantages of preliminary colostomy for rehabilitation and greater security in correction of the fistula?

It is proposed, therefore, that the standard treatment for gastrojejunocolic fistula consist

of preliminary colostomy to be followed at an appropriate interval by subtotal gastric resection with the necessary repairs or anastomoses to re-establish continuity. A simultaneous jejunostomy by the simple purse-string method may be an advantage. Or in its stead the double lumen tube passed through the anastomosis will insure against distention and afford an avenue for fluids later, if needed. Naturally, parenteral fluids, transfusions as indicated, and careful chemical balance are essential in every case. Ascending colostomy through an oblique loin incision is suggested as answering the purpose and being well away from the field of the second stage. A left rectus or paramedian incision should be made for exploration of the lesion. If conditions seem to favor the one stage radical operation, it may be chosen but the surgeon must remember that he will be working in a field contaminated by infection from the colon. If preliminary colostomy is made, the exploration will at once reveal the site best available and as distant as possible from the field of the second stage. No serious exception can be taken to complete cecostomy or right transverse colostomy. Harvey chose ileostomy but this is less suitable if a considerable interval is to elapse, as it must in depleted patients. Concerning the interval, it is usually a matter of weeks or months before maximum improvement has occurred and the second stage should not be hurried.

#### SUMMARY AND CONCLUSIONS

In summary then it may fairly be concluded that

- 1 The most serious consequences of gastrojejunal fistula arise from admission of colonic contents to the stomach and jejunum rather than from loss of food from stomach through the fistula

- 2 Loop colostomy proximal to the fistula is the best means of relieving symptoms and facilitating rehabilitation

- 3 Preliminary colostomy permits subsequent correction of the fistula by the necessary radical measures in a clean field and protects the repair of the colon

- 4 The operative mortality, 6.6 per cent, is shown to be greatly reduced by this plan



# THE SURGICAL TREATMENT OF ACHALASIA OF THE ESOPHAGUS

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THE term achalasia, applied to the clinical syndrome characterized by dilatation and hypertrophy of the esophagus with non-organic obstruction of the cardia, is employed with the full realization of its pathogenic significance. Numerous other designations such as, cardiospasm, phrenospasm, esophagectasia, mega esophagus, idiopathic dilatation of the esophagus, etc., have been used clearly reflecting the controversial opinions regarding the etiology of this distressing malady. No attempt will be made here to discuss these various theories as they have been adequately reviewed in previous publications (3, 4, 21, 51, 68, 71, 72). However we are inclined toward the pathogenic concept which is implied by the term achalasia.

The surgical importance of this condition is not sufficiently realized and has been minimized probably too greatly. Although its incidence is not high it occurs with sufficient frequency to deserve more intensive consideration. Moersch (47) considers it one of the most common diseases of the esophagus. Guisez, in 1935 stated that during the previous 6 years he had examined esophagoscopically 946 patients and of this number 165 or 17.4 per cent, had achalasia. With the exception of carcinoma it was the most frequent cause of esophageal obstruction. This observation has also been made by other investigators (8, 76). Achalasia comprised 17.8 per cent of esophageal lesions in Walton's series. At the Mayo Clinic more than 200 cases have been observed (6). Undoubtedly in the majority of cases patients can be treated conservatively but a certain number will require surgical intervention. Of 805 patients treated conservatively by Moersch (48) 71 per cent

were completely relieved. However Walton and Hill were unable to obtain such a high incidence of good results by these more conservative methods. In Wachs' series of 52 cases, 16 or 30.3 per cent, required surgical therapy. Thus, it may be stated that a little less than a third of the cases will not be completely relieved by conservative measures and the majority of these will probably necessitate more radical therapeutic procedures. Whereas every patient should be given the benefit of conservative treatment first, if such measures do not accomplish adequate relief of symptoms in a reasonable period of time surgical intervention should be considered. Undoubtedly in the past there has been too great a reluctance on the part of the physician to institute such measures with the result that many patients who could be cured have been permitted to continue having distressing manifestations for years and even to develop irreparable complications. This has been due to some extent to the prevalent impression that the risk of operative therapy is considerably greater than of conservative therapy. Actually however the mortality of the latter is only slightly less than the former. In Moersch's (48) series of 804 patients treated conservatively 9 died from splitting of the esophagus, 2 died of starvation, and 12 died at home. Of 239 collected cases in which cardioplasty and esophagostomy were the procedures performed there were 10 or 4.2 per cent, deaths (51).

The varied procedures that have been advocated and employed in the surgical treatment of achalasia clearly reflect the diversity of opinion and the conflict of views regarding the etiology and pathogenesis of this condition.

In a previous publication reviewing the subject (51) these procedures were classified as follows:

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- I Operations directed at the dilated esophagus
  - A Excision of wall
  - B Esophagoplication
  - C Esophagostomia thoracica
- II Operations directed at the cardia
  - A Dilatation
    - 1 Retrograde
    - 2 Transgastric
  - B Plastic
    - 1 Cardiomyotomy
    - 2 Cardioplasty
  - C Excision
    - 1 Cardiectomy
  - D Deviation
    - 1 Esophagogastrostomy
- III Operations directed at the diaphragm
  - A Phrenotomy
  - B Transposition
- IV Operations directed at the nerve supply
  - A Vagotomy
  - B Sympathectomy

It is considered inexpedient to attempt here a detailed presentation of all these surgical therapeutic measures as they have been adequately reviewed in a previous publication (51). However, it may be desirable to indicate briefly the rationale of these procedures and to describe succinctly their nature. Those having the most rational basis in our opinion will be considered in greater detail.

Based upon the assumption that an artificial reduction in size of the markedly dilated esophagus would correct the condition, Jaffé, in 1897, suggested excision of long strips of the esophageal wall and closure of the resultant defects. This was first performed by Reisinger, 10 years later. Based upon a similar rationale, Meyer (36, 37), in 1911, performed esophagoplication by suturing together two longitudinal folds of the esophageal wall. In addition to this Meyer did a vagolysis. Because of the poor results obtained in 3 cases Meyer (38-40) concluded that a plastic procedure similar to the Heineke-Mikulicz pyloroplasty was preferable. Freeman's procedure, based upon artificial reduction in length rather than width, consisted of exposing the esophagus through a cervical wound and pulling upward on it until the portion below was "rendered quite taut" and then invaginating the upper segment into the lower so that an intussusception was produced. Zaaier's (81) procedure consisted of gastrostomy and then esophagostomy after preliminary thoraco-

plasty to bring the chest wall nearer the esophagus. In this way everything the patient swallowed was discharged through the esophageal opening, collected, and then emptied into the stomach through the gastrostomy.

These procedures attacking the dilated esophagus are obviously irrational and at present are of historical interest only. Because the obstruction to the passage of food is apparently at the cardia, operative procedures directed at this structure seem to have a more rational basis. As early as 1882, von Mikulicz (41) had propounded the concept reflected by the term *cardiospasm* and had drawn the analogy between this and spasm of the anal sphincter associated with a fissure. It seemed logical, therefore, to assume that dilatation of the cardia would be a rational corrective procedure, and, in 1903, von Mikulicz (42-44) performed this operation which consisted of exposing the stomach through a laparotomy incision and introducing into the cardia an instrument resembling a glove stretcher through an incision in the anterior wall of the stomach. In this manner, he was able to stretch the cardia until he could introduce two or three index fingers through it very readily. The procedure was modified by Rotgans who performed the dilatation by forcefully invaginating the anterior wall of the stomach up through the cardia in order to avoid possible peritoneal contamination by opening the stomach. In a previous publication (51) we collected from the literature 80 cases in which patients were treated in this manner. Of this number good results were reported in 70.8 per cent, failures in 10.1 per cent, and deaths in 8.9 per cent. The procedure is obviously not without danger and accomplishes little more than dilatation by the natural oral route.

Mikulicz's view that a true spasm of the cardiac sphincter existed in this condition widely prevailed at the turn of this century. Under this influence, Gottstein, in 1901, proposed extramucous cardiomyotomy similar to the Ramstedt procedure for hypertrophic pyloric stenosis. However, this operation was not performed until 12 years later by Heller. Whereas some (17, 82) subsequently stated that one incision was sufficient Heller emphasized the necessity of two longitudinal in-

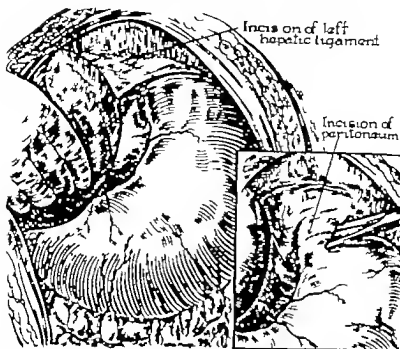


Fig. The technique of esophagogastrostomy in treatment of achalasia which prefer Through high left paracostal or left subcostal incision the left lateral hepatic ligament is exposed and divided. This permits retraction of the left lobe of the liver and better exposure of the cardia. The peritoneum over the esophagus is incised at the site of its reflection on the diaphragm as illustrated in the inset.

cisions, one anterior and one posterior. Of 104 cases collected by the authors (51) in which this procedure was done the results were reported as good in 76.9 per cent, improved in 5.7 per cent, recurrences in 13.4 per cent, and the mortality was 3.8 per cent.

Another plastic procedure first suggested by Marwedel, in 1903 and performed by Wendel, 7 years later is analogous to the Heineke Mikulicz (13-14) pyloroplasty. Whereas this procedure consists of incising longitudinally through the entire wall of the cardia and suturing the defect transversely the modification proposed by Girard, in 1915 is analogous to the Fredet-Weber (9-79) type of pyloroplasty and consists of incising longitudinally only down to the mucosa and then suturing the resultant defect transversely. The obvious purpose of the latter procedure is to avoid the opening of the lumen with consequent peritoneal contamination. Of 36 cases collected from the literature in which cardioplasty was

performed good results were reported in 93.1 per cent, recurrence in 2.8 per cent, and the mortality was 2.8 per cent (51).

The procedure of excision of the cardia followed by esophagogastrostomy was originally proposed by Rumpel, in 1897 but was not taken seriously until 23 years later when Bier performed the operation in a case reported by Pinbam (55). Such a radical procedure is hardly justified in the presence of a benign lesion. In our opinion the procedure deserving the most consideration and based upon the soundest rationale is esophagogastrostomy. This may be performed as a side-to-side anastomosis between the esophagus and stomach thus short-circuiting the cardiac orifice or preferably in a manner similar to the Finney gastroduodenostomy. The former was originally done by Heyrovsky in 1912 and the latter by Gröndahl in 1916 although Lambert, in 1913 had accomplished the same end by crushing the spur with forceps. The objec-

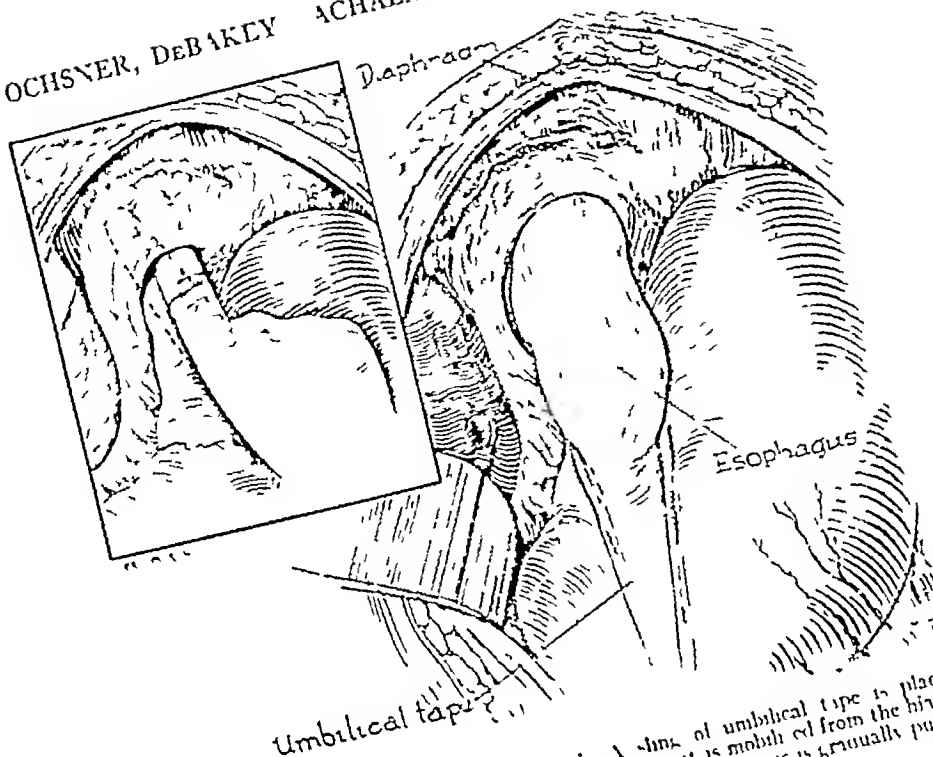


Fig. 2. Esophagogastrostomy continued. A strip of umbilical tape is placed around the esophagus to permit traction downward as it is mobilized from the hiatus by blunt dissection with the finger. In this manner the esophagus is gradually pulled down into the peritoneal cavity for a distance of about 10 centimeters.

tion to the former procedure of side-to-side anastomosis is the presence of a spur which, as emphasized by Levy, may produce some obstruction to the free passage of food from the esophagus into the stomach. In the latter type of anastomosis this cardiac spur is destroyed and a much wider opening is created between the stomach and esophagus thus permitting free emptying. This method is preferred by us and has been successfully employed in 2 cases previously reported (51). In addition to these we (51) collected from the literature 88 cases in which esophagogastrostomy was done. More recently Wachs has reported 9 other cases making a total of 97 collected cases in which patients had a poor result and the remainder had excellent results. Numerous surgeons have directed attention to the highly interesting feature of the results of this operation as well as some of the other procedures. It is to be observed

that the functional results following operation are considerably better than the roentgenological studies would indicate. This is exemplified to some extent by one of our patients who following operation has remained completely relieved of all previous manifestations. Whereas roentgenograms of the esophagus reveal a decrease in size there is still some dilatation.

The procedure of esophagogastrostomy may be done either through a trans-abdominal or a trans-thoracic approach. No attempt will be made here to discuss the various approaches as they have been described and critically analyzed in previous publications (50, 51). In our opinion the trans-abdominal approach is considered the most desirable and can be done either through a lateral or a pararectal incision or a midline incision on paralleling the costal margin. Adequate exposure of the cardia is readily obtained by division of the left latissimus dorsi muscle and upward traction of

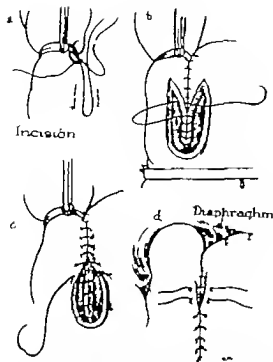


Fig. 3. a. A strip of umbilical tape is tied tightly around the uppermost portion of the mobilized esophagus. This serves a twofold purpose: (1) It prevents spillage from the esophagus above during the anastomosis, and (2) It acts as a means of anchoring the fundus of the stomach to the esophagus by placing the anchor suture around the tape, thus avoiding tearing the friable esophageal wall. b. After the first posterior row of interrupted quilting cotton sutures is placed, an incision is made paralleling this row of sutures, through the stomach and esophagus and carried through the cardia as indicated by the dotted line m. The second posterior row of sutures is applied as a continuous through-and-through stitch. No. 00 chromic catgut is used on an atraumatic needle and brought anteriorly as Connell stitch. c. The final row of interrupted Lambert cotton sutures. A few interrupted cotton sutures are used to tack the diaphragm to the esophagus and to the fundus of the stomach in order to avoid traction on the suture line.

the left lobe of the liver as suggested by Lambert (Fig. 1). After the peritoneum is incised over the esophagus at the site of its reflection on the diaphragm, the esophagus is freed circumferentially by sharp and blunt dissection. A sling of umbilical tape is placed around the esophagus to permit traction downward as it is mobilized from the hiatus by blunt dissection with the index finger (Fig. 2). In this manner the esophagus is gradually pulled down into the peritoneal cavity for a distance of about 10 centimeters. A strip of umbilical

tape is tied tightly around the uppermost portion of the mobilized esophagus (Fig. 3 a). This excellent technical suggestion of Fromme serves a twofold purpose: (1) It prevents spillage from the esophagus above during the anastomosis and (2) it is a means of anchoring the fundus of the stomach to the esophagus by placing the anchor suture around the tape, thus avoiding tearing the friable esophageal wall (Fig. 3 a). After the first posterior row of interrupted quilting cotton sutures are placed (52-53) an incision is made paralleling this row of sutures, through the stomach and esophagus and carried through the cardia (Fig. 3 a and b). The second posterior row of sutures is applied as a continuous through-and-through stitch, No. 00 chromic catgut on an atraumatic needle being used, and is then brought anteriorly as a Connell stitch (Fig. 3, b and c). This is followed by a final row of interrupted Lambert cotton sutures (Fig. 3 d). A few interrupted cotton sutures are used to tack the diaphragm to the esophagus and to the fundus of the stomach in order to avoid traction on the suture line (Fig. 3 d). The strip of umbilical tape tied around the esophagus is cut and removed. Reinforcement of the anastomotic line by an omental graft as suggested by Palugray (54) may be done.

Operative procedures directed at the diaphragm are based upon the concept, originally postulated by Sauerbruch and Hacker, that the condition is the result of overactivity, a failure of relaxation, or an inco-ordination of the diaphragmatic crura. This theory is reflected in the term "phrenospasm" proposed by Jackson. On this basis, Baseler in 1914 suggested division of the diaphragmatic crura. Vampre, who obtained consistently poor results following this procedure, finally concluded that it was irrational. In 1913 von Hacker (20) suggested in addition to enlarging the diaphragmatic hiatus, drawing the esophagus down and straightening it out. Because Turner (73-74) obtained only 1 good result in 5 cases he finally discontinued using this operation.

Surgical procedures directed at the nerve supply of the esophagus in the treatment of achalasia are based upon certain clinical and experimental observations which have been

presented in an attempt to explain the pathogenesis of this condition on the basis of a nervous mechanism. A detailed discussion of these numerous observations which form the basis of this concept is considered inopportune here and the reader interested in this phase of the subject is referred to a previous publication (51). Suffice it to say that in general they may be classified into those incriminating the vagus and those incriminating the sympathetics. Accordingly, the surgical attack has been directed at these respective innervations. Vagotomy was performed by Meyer, in 1911, in addition to esophagoplication but because the results were poor he finally concluded that the procedure was of no value. Similar results were obtained by Sauerbruch (65, 66), Rieder, and Jirasek. Of 11 collected cases in which vagotomy was done, only 1 had a satisfactory result. At present the procedure appears to be of historical significance only.

Probably the first to attack the sympathetics was Récalde (58, 59), who, in 1924, advocated decortication of Auerbach's plexus. He performed this operation on 4 patients and obtained a good result in 3. Ten years later, Knight (28, 29), on the basis of extensive experimental investigations, placed sympathectomy in the treatment of achalasia on a firmer foundation. Performing his experiments on cats because the neuromuscular mechanism of the esophagus in these animals more closely resembles that of humans, he was able to demonstrate the presence of a true sphincter mechanism at the cardia. Moreover, he showed that bilateral vagal section reproduces the clinical and pathological picture of achalasia and that the condition can be relieved by sympathectomy. He also showed that in the human, the sympathetic supply to the cardiac sphincter is derived chiefly from the left side of the celiac plexus and distributed along the left gastric artery. Accordingly he advocated sympathectomy by excision of this artery and the surrounding fat and nervous tissue. Of 5 patients operated upon in this manner by Knight (30, 31) and Adamson, 1 was completely relieved, 1 was considerably improved, and the 3 others showed signs of recurrence. Since then others (6, 35, 64, 69, 70) have reported the use of this treatment but the re-

sults in their cases have not been very impressive. A somewhat different technique of sympathectomy was done by Craig, Moersch, and Vinson. These authors reported a good immediate result in a case of achalasia treated by bilateral resection of the cervicothoracic sympathetic ganglia and trunk. We used a similar technique in a case previously reported in which a diagnostic procaine hydrochloride block by the anterior approach (49) was followed by rapid passage of barium through the cardia as determined fluoroscopically. Whereas immediate improvement followed the operation, several weeks later there was complete recurrence. Recently Mitchell stated that the high incidence of failures following sympathectomy may be explained on the basis of the great anatomic variation in the sympathetic supply to the cardia and the consequent difficulty of completely interrupting these pathways.

#### SUMMARY

1 The surgical significance of achalasia is emphasized. Whereas the majority of patients can be effectively treated by conservative measures, slightly less than a third will require surgical intervention.

2 A number of surgical procedures have been devised and advocated and may be classified in 4 groups: (1) those directed at the dilated esophagus, (2) those directed at the cardia, (3) those directed at the diaphragm, and (4) those directed at the nerve supply.

3 The rationale of these various procedures is indicated briefly and their nature succinctly described.

4 In our opinion the procedure deserving the most consideration and having the soundest rationale is esophagogastrostomy. The preferable technique is described and illustrated.

#### BIBLIOGRAPHY

- 1 ADAMSON, W. A. D. Sympathectomy for achalasia of the cardia. *Proc Roy Soc Med*, 1934-35, 28: 892.
- 2 BASSLER, A. Cardiospasm. What is it? What it seems to be. *New York State J Med*, 1914, 14: 9.
- 3 BIRD, CLARENCE E. Recent advances in surgery of the esophagus. *Surgery*, 1939, 6: 617.
- 4 BULL, P. N. So-called idiopathic dilatation of the esophagus. *Ann Surg*, 1925, 81: 59, 470.
- 5 CRAIG, W., MOERSCH, H. J., and VINSON, P. P. Treatment of intractable cardiospasm by bilateral cer-

- vicathoracic sympathetic ganglionectomy report of case. Proc. Staff Meet. Mayo Clin., 1934, 9, 749.
6. ELLIOTT, E. L. and EMM, W. H. Cardiospasm report of two cases treated by resection of sympathetic supply to the cardiac sphincter. *Ann. J. Surg.* 1937, 35, 95.
  7. FERRY, J. M. T. A new method of pyloroplasty. *Bull. Johns Hopkins Hosp.* 1904, 3, 35.
  8. FRYER, RICHARD. Achalasia of the esophagus. *Australas. & New Zealand J. Surg.* 1930, 8, 244.
  9. FUCHET. La sténose hypertrophique du pylore chez le nouveau-né. *Arch. d'anal. de l'appar. digest.* 1908, 303.
  10. FREEDMAN, L. An operation to relief of cardiospasm associated with dilatation and tortuosity of the esophagus. *T. Am. Surg. Ass.* 1932, 4, 9.
  11. FRIED, E. K. Zur Behandlung des Kardiospasmes. *Arch. f. klin. Chir.* 1930, 86, 466.
  12. FROEYER, A. Ueber Ursachen und Behandlungsmethoden des sogenannten Kardiospasms auf Grund klinischer Erfahrung. *Beitr. klin. Chir.* 1935, 62, 237.
  13. FROMMELT, F. Operation der Pylorostomie. In *Original Dissertation*, Jena, 1886.
  14. GILARD. Quoted by Hacker and Lotheissen ( ).
  15. GÖTTSCHEW, G. Technik und Klinik der Oesophago-skopie. *Mitt. d. Grenzgeb. d. Med. Chir. Jena*, 1901, 3, 57, 99, 5.
  16. GRA, HOWARD L., and SEITZ, J. C. The operative treatment of cardiospasm. *J. Thoracic Surg.* (In press.)
  17. DE BRUNDE GROOTVELDT, J. B. Over cardiospasmus. *Nederl. T. Idsch. Geneesk.* 1918, 251.
  18. GRÖNMAN, N. B. Cardiosplastik und Cardiospasmus. *Nord. Med. Arkiv.* 1916, 40, 36.
  19. GROSS, J. V. Fréquence relative des différentes affections de l'oesophage d'après la statistique des cas observés dans ces dix dernières années. *Bull. et méém. Soc. de chir. de Par.* 1935, 7, 331.
  20. VO HÄCKER. Quoted by Hacker and Lotheissen ( ).
  21. VON HÄCKER, V., and LOTZKE, G. Chirurgie der Speiseröhre. *St. Hippert F. Enke* 1906.
  22. HILLER, E. Extralukale Cardiosplastik beim chronischen Cardiospasmus mit Dilatation des Oesophagus. *Mitt. d. Grenzgeb. d. Med. Chir.* 1913, 14, 27, 4.
  23. HETROVSKY, H. Casuistik und Therapie der klobopathischen Dilatation der Speiseröhre, Oesophago-gastroanastomose. *Arch. f. klin. Chir.* 1912, 9, 2-43, 100, 703.
  24. HILL, W. Discussion on dilatation of esophagus with other anatomical stenosis. *Proc. Roy. Soc. Med.* 1911, 9, 33.
  25. JACKSON, C. The diaphragmatic Pinchcock in presence of so called "cardiospasm." *Laryngoscope*, 1922, 3, 39.
  26. JÄTTI, A. Ueber klobopathische Oesophagusverengung. *München. med. Wchnsch.* 1907, 44, 386.
  27. JERABEK, A. U cas d'oesophago-gastro-anastomose réussie. *Bull. et méém. Soc. nat. de chir.* 1913, 39.
  28. KROGER, G. C. The relation of the extrinsic nerves to the functional activity of the esophagus. *Brit. J. Surg.* 1914-35, 35.
  29. Idem. The innervation of the esophagus. *Proc. Roy. Soc. Med.* 1934-35, 28, 89.
  30. Idem. Sympathectomy in the treatment of achalasia of the cardia. *Brit. J. Surg.* 1934-35, 22, 854.
  31. Idem. Sympathectomy for achalasia of the cardia. *Proc. Roy. Soc. Med.* 1934-35, 28, 877.
  32. LAMBERT, A. W. S. Treatment of diffuse dilatation of the esophagus by operation. Description of kuhner's unpublished method, report of case. *Surg. Gynec. & Obst.* 1914, 8.
  33. LOTZKE, G. Quoted by Hacker and Lotheissen ( ).
  34. MARWITZ, GROSZ. Die Anknüpfung des Rappensystems zur Erleichterung operativer Eingriffe im Hypochondrium und im Z. erchfeldapparat. *Zentralbl. f. Chir.* 1903, 30, 928.
  35. MARIAS, H. S. A case of sympatheticlectomy in the treatment of achalasia of the cardia. *Idsch. J. M. Sc.* 1904, 30, 30.
  36. MEYER, WILL. Impermeable cardiospasm successfully treated by thoracotomy and esophagoplication. *Ann. Surg.* 1913, 55, 203.
  37. Idem. Impermeable cardiospasm successfully treated by thoracotomy and esophagoplication. *J. Am. M. Ass.* 1914, 55, 437.
  38. Idem. Thoracotomy for impermeable cardiospasm (14 cases). His remarks on drainage after intra-thoracic operations. *Ann. Surg.* 1915, 55, 326.
  39. Idem. Operative treatment of intractable cardiospasm. *Am. J. Surg.* 1916, 20, 93.
  40. Idem. Discussion of Lambert. *Ann. Surg.* 1916, 55, 47.
  41. ON MIXELT, J. Ueber von Gastrostomie Oesophagostomie. *Mitt. d. Ver. d. Aerzt. in Nied.-Oest.* 1900, 25, 2.
  42. Idem. Small contributions to the surgery of the intestinal tract. *Boston M. & S. J.* 1903, 148, 608.
  43. Idem. Zur Pathologie und Therapie des Cardiospasmus. *Deutsche med. Wchnsch.* 1904, 30, 90.
  44. Idem. Zur Pathologie und Therapie des Cardiospasmus. *Deutsche med. Wchnsch.* 1904, 30, 90.
  45. Idem. Behandlung des stenotischen Magenspiasmus. *Arch. f. klin. Chir.* 1883, 37, 70.
  46. MITCHELL, G. A. G. The nerve supply of the gastro-esophageal junction. *Brit. J. Surg.* 1938, 26, 113.
  47. MORGAN, HENRY J. Cardiospasm in infancy and in childhood. *Am. J. Dis. Child.* 1930, 38, 394.
  48. Idem. Cardiospasm its diagnosis and treatment. *Ann. Surg.* 1932, 95, 32.
  49. OCHSNER, ALTON and DEBAKEY, MICHAEL. Treatment of thrombophlebitis by novocain block of sympathetic. *Surgery* 1930, 5, 401.
  50. Idem. Carcinoma of the esophagus. *J. Thoracic Surg.* (In press.)
  51. Idem. Surgical considerations of achalasia, review of the literature and report of three cases. *Arch. Surg.* (In press.)
  52. OCHSNER, ALTON and MERRILL, WILLIAM. Spool test on suture material. *J. Am. M. Ass.* 1930, 3, 2190.
  53. Idem. The relative value of catgut, silk, linen, and cotton as suture materials. *Surgery* 1929, 7, 483.
  54. PALATY, J. Die Oesophago-gastro-anastomose nach Heyrovsky im Röntgenbild. Ein Beitrag zum funktionellen Verhalten der Speiseröhre und des Magens nach der Operation. *Arch. f. klin. Chir.* 1923, 5, 554.
  55. PRINGS, H. O. Zur Pathologie und Chirurgie der sympathischen Nerven. *Arch. f. klin. Chir.* 1900, 30, 207.
  56. Idem. Discussion of Krukenberg's paper. *Verhandl. d. deutsch. Gesellsch. f. Chir.* 1911, 45, 47.
  57. RANBY, C. Zur Operation der angeborenen Pylorostomie. *Monatsh. f. Klin. Chir.* 1911, 400.
  58. RICALDE, J. F. Sobre un caso de mal de esófago curado cirurgicamente. *Bol. Soc. de ped. chir. de S. Paulo*, October, 1924.

- 59 Idem. Cardiospasm, disfagia e megaresofago, simpaticotomia esofagica (statistica chirurgica) Arch ital di chir, 1932, 32 613
- 60 REISINGER Ueber die operative Behandlung der Erweiterung des Oesophagus Verhandl d deutsch Gesellsch f Chir, 1907, 36 86
- 61 RIEDER, E Klinik und Therapie des sogenannten Cardiospasmus Deutsche Ztschr f Chir, 1930, 222 47
- 62 ROTGANS Quoted by Zaaier, J H On Surgery of the esophagus Cong de la Soc internat de chir, 1932, 1 485
- 63 RUMPEL, T Die klinische Diagnose der spindel foermigen Speiserohrenverweiterung Muenchen med Wehnschr, 1897, 44 383
- 64 RUPP Discussion of I rey's case. Arch f klin Chir, 1936, 186 19
- 65 SAUERBRUCH, I Discussion of Kuemmel Verhandl d deutsch Gesellsch f Chir, 1921, 45 149
- 66 Idem Chirurgie der Brustorgane Vol 2, Der Kardiospasmus, page 572 Berlin Julius Springer, 1925
- 67 SAUERBRUCH, I, and HACKER, R Zur Frage des Cardiovascularschlusses der Speiserohre Deutsche med Wehnschr, 1906, 32 1263
- 68 SODEMAN, WILLIAM A Cardiospasm or achalasia of the esophagus Am J M Sc, 1940, 190 132
- 69 SOUTTAR, H S Oesophageal obstruction Brit M J, 1935, 2 777
- 70 STRUBBE, H Oesophageal achalasia treated by sympathectomy Med J Australia, 1937, 2 1001
- 71 STURTEVANT, M Cardiospasm with a review of the literature Arch Int Med, 1933, 51 714
- 72 THIEDING, I Ueber Cardiospasmus, Atonie und "Idiopathische," Dilatation der Speiserohre Beitr z klin Chir, 1921, 121 237
- 73 TURNER, G G Some experiences in the surgery of the esophagus New England J Med, 1931, 205 657
- 74 Idem. Personal experience in the surgery of the lower esophagus Cong de la Soc Internat de chir Rap, 1932, 1 725
- 75 VAMPRE, L Le "Mal de Engasgo" et son traitement chirurgical Rev sud am de med et de chir, 1933, 4 493
- 76 VINSON, PORTER B The diagnosis and treatment of cardiospasm J Am M Ass, 1924, 82 859
- 77 WACHS, L Ueber Methoden der Kardiospasmusbehandlung und ihre Erfolge, 64 Tag d deutsch Ges f Chir, Berlin, 1940
- 78 WALTON, A J The surgical treatment of cardiospasm Brit J Surg, 1925, 12 701
- 79 WEBER, W Ueber eine Technische neuerung bei der Operation der Pylorusstenose des Sauglings Berl klin Wehnschr, 1910, 47 763
- 80 WFNDEL, W Zur Chirurgie des Oesophagus Arch f klin Chir, 1910, 93 311
- 81 ZAAIJER, J H Oesophagotomia thoracalis Beitr z klin Chir, 1912, 77 497
- 82 Idem Cardiospasm in the aged Ann Surg, 1923, 77 615



## SOME FACTORS INFLUENCING THE CURABILITY OF CANCER OF THE STOMACH

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**A** MOST recent report on deaths from all causes by the Bureau of the Census shows during the period 1920 to 1938 a steady and inexorable increase from year to year in the percentage of deaths from cancer. This is true of no other cause of death listed. Even diseases of the heart and accidental deaths, while larger in total amount, show a variation from year to year. Cancer of the stomach is one of the most depressing phases of this whole subject and constitutes a large part of the clinical problem of cancer. It comprises 35 per cent of all cancer causes, one third of all cancer deaths, and results in more than 100 fatalities every day in the year.

The problem is receiving increasing thought as is shown by the ever-growing number of articles written upon the subject, an average of 175 titles annually for the past few years. Thus, an enormous amount of information bearing on the incidence, pathology, treatment and statistics has been accumulated. It is probable that cancer of the stomach rarely occurs in the normal stomach, and also that the various types of chronic gastritis, atrophic and hyperplastic, are frequent precursors. To speak of irritation alone as a cause is not sufficient unless another factor, susceptibility, which is probably inherited, be added. The chemists have shown the importance of the common factor in the synthetic carcinogenic compounds, the phenanthrene ring system. Among the substances occurring naturally in the body and containing this particular ring system are ovarian hormone, male hormone, cholesterol and the bile acids. From one of these, dioscholic acid, Cook synthesized methylcholanthrene, a strongly carcinogenic agent, and Needham suggests that from normally occurring compounds a deranged metabolism may produce specific carcinogenic

substances in the body. There is high estrogenic activity in many synthetic hydrocarbons whose carcinogenic activity has long been known (11) and this may be suggestive in view of the fact that cancer of the stomach occurs most frequently in the male and at the involuntarily period. There is much conflict in the literature, the general attitude being one of pessimism and the impression given is that under the present conditions the disease is hopeless for over 95 per cent of its victims. That the situation is not so entirely desperate, however, is revealed by the number of reports of cures of 10 or more years after surgical excision of the growth. In a large number of cases without metastasis 48 per cent were living 5 years after resection (3) and that there are many more who die without the chance of being included in this group is shown by Warwick's study that in 13 per cent death intervened before metastasis occurred. When the neoplasm was still confined to the stomach, 50 per cent of all patients upon whom resection was done were alive 5 years later and 90 per cent of patients examined 10 years or more after resection were found to be living normal lives (33). The other side of the picture and that which leads to the general pessimistic attitude is drawn by Maes, Boyce and McFetridge, Saltzstein and Sandwels, and most recently by Abrahamson and Hinton, who found that out of the total number of cases seen only 4.6 per cent, 7.4 per cent and 5.4 per cent respectively were amenable to surgical treatment. It is very probable that these latter figures closely approximate the true situation for the country at large. There are many other reports equally gloomy and the vast majority of surgeons must admit that they have never seen a cure of gastric cancer in their own practice.

Owens estimates that there are 450,000 persons with cancer now living in the United States. One third of this great number or

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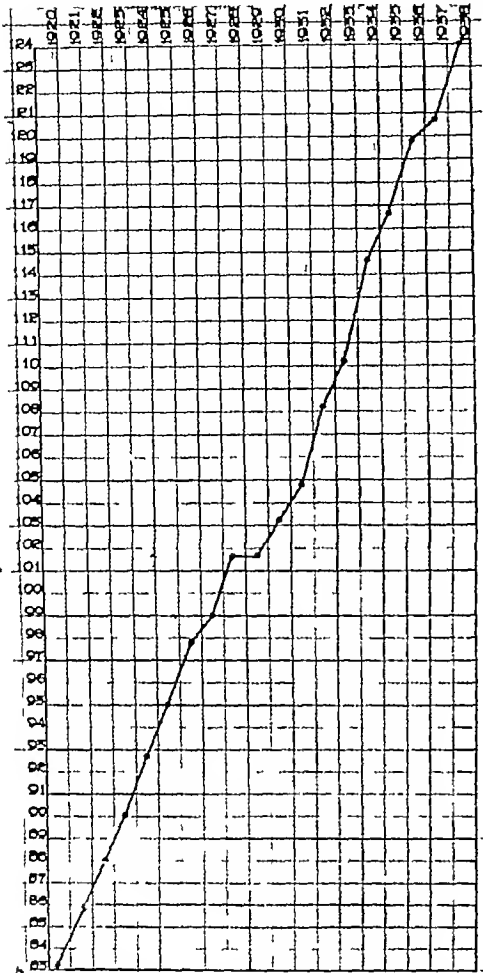


Fig 1 Cancer death rates Number per 100,000 estimated population, Bureau of Census 1940, vol 9, p 849

150,000, should approximate the number of cases of gastric cancer. If the average percentage of resectable tumors is 18, there are probably 27,000 resectable gastric cancers in the country at this time. Pack and Livingston estimate the number as in excess of 10,000 and the truth is somewhere between these two figures. The small part of these potentially curable patients who are given their chance for cure is shown by the fact that only 3,000 gastric resections have been reported in the United States during the 50 years of gastric surgery while in the same period 1,500,000 persons have died of the disease (33).

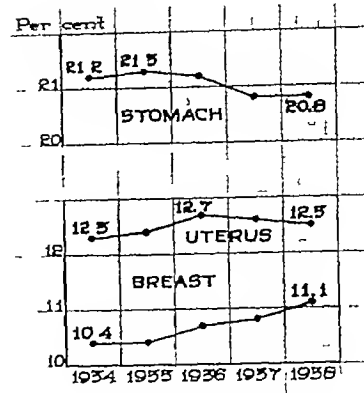


Fig 2 Death rate per 100,000 estimated population

It is quite evident that in spite of repeated emphasis placed upon the subject the public is not yet conscious of its serious import, and the profession is not using to the greatest advantage all of the information at its command. The cure of disease ordinarily depends almost entirely on the spontaneous power of the organism to repair itself. Our therapeutic efforts only set the mechanism in motion, and, since natural defenses against the cancer cell are usually not marked in gastric cancer, our therapeutic efforts must be instituted before all power of repair is completely lost. In cancer, as in other diseases, there is an acute and a chronic form, although we are very prone to overlook the possibility of the latter's existence.

We speak of the inoperability of cancer of the stomach after symptoms of a few weeks' duration as though the process dated from the onset of those symptoms, when in reality it is much older. In many cases the consciousness of symptoms comes only after they have repeatedly recurred and gradually become intensified. Limitation of the growth to the stomach does not necessarily mean that it is of recent origin (27). A pre-invasive state may exist for a long time and mild and unrecognized symptoms might be thus explained. The fact that cancer begins in the stomach as a limited disease and may persist thus for a long time has been stressed by MacCarthy, who now thinks that this occurs more frequently than he originally stated. The occurrence of a long history has frequently been noted in

young patients by Friedell. Factors then which influence the curability of the disease are those which make possible the recognition and the prompt surgical treatment of the process during this stage. These factors pertain first to the patient and second to the physician and may be considered under the alliterative headings of (1) a sensitive patient (2) a suspicious clinician (3) a studious and searching roentgenologist and gastroscopist (4) a super-skillful surgeon.

**The sensitive patient** It is a fact that most persons consider a mild degree of gastric discomfort to be a part of the normal process of growing older and the words "indigestion" and "dyspepsia" to most minds signify an uncomfortable but entirely benign process. Yet within these two words is the whole story of early gastric cancer symptomatology. It is quite necessary that the public be impressed with the dangerous significance of the symptoms of indigestion and dyspepsia, and while there is some danger of creating a cancer phobia, that in itself would not be an entirely evil thing. Rivers in a study of a large group presenting dyspepsia as the main symptom found up to 14 per cent of carcinoma in females and up to 36 per cent in males from 40 to 70 years of age. In a study of the various reports upon the early symptoms of cancer of the stomach it is noted that there is a predominance of those symptoms which are usually called "indigestion or dyspepsia." Devine describes 12 different forms that this may take. The diagnosis of early cancer of the stomach cannot be made on clinical factors alone but it is necessary to make a tentative diagnosis based upon an early recognition of symptoms which are suggestive. In order to have these brought to our attention it is necessary that the patient be sensitive enough to notice them and he must be taught that (1) the abrupt onset of dyspepsia in a person who has been well previously (2) epigastric distress, (3) loss of appetite or a change in food desire, (4) weakness, and (5) an unusual family history of cancer are suggestive and ominous signs which should be reported to us.

Symptoms listed by various authors include those of late as well as those present in early disease.

Gatewood (39 per cent, 58 of 47 resected)	Labrey (5.7 per cent, 30 of 105 resected)
1. Pain	1. Indigestion
2. Loss of weight	2. Anorexia
3. Vomiting	3. Pain
4. Weakness	4. Weight loss
5. Indigestion and belching	5. Vomiting
6. Loss of appetite	6. Dysphagia
7. Fullness	7. Weakness
8. Anemia	8. Hemorrhage
9. Regurgitation	9. Constipation
Oughterson (58 per cent, 9 of 30 resected)	Ransom and Collier (34 per cent, 65 of 45 resected)
1. Abdominal discomfort	1. Epigastric pain
2. Loss of weight	2. Anorexia
3. Constipation	3. Pain and gas
4. Eructation	4. Pain and weakness
5. Anorexia	5. Pain and vomiting
6. Vomiting	6. Nausea and swelling
7. Regurgitation	7. Stomach trouble
8. Diarrhea	8. Dyspepsia
Harris	
1. Gradually increasing loss of appetite	9. Gas
2. Epigastric distress	10. Abdominal distention and dyspepsia
3. Indistinct abdominal pain	11. Nausea and distension
4. A history of ulcer with change in intensification of symptoms	12. Vomiting of blood
5. Gradual loss of weight	13. Dysphagia
6. A family history of cancer	14. Pain and tumor
7. A little loss of weight	15. Loss of weight
8. Anemia	16. Vomiting and exsanguination
	17. Fatigability and pain

Most of these symptoms could be truly called those of simple dyspepsia. Those underlined are not usually due to early disease which was evidently not common in the cases upon which these lists are based, as is seen in the percentage of resectability. The prevalent ideas of the symptomatology of the disease is based on more or less advanced cases. If the diagnosis is to be made while the patient is still well as it must be if we will influence the curability he will have to be educated to the need of being sensitive to mild degrees of gastric discomfort, and he will fall into one of three classes (1) those who have never had digestive disturbances before, (2) those who have had previous digestive disturbance due to either organic disease or functional disturbance, or (3) those who have no digestive disturbance but rather complain of some debilitating disease. The patient who is sensitive to mild degrees of digestive discomfort is not the

emaciated, cachectic, and vomiting person who has suffered from pain and increasing distress for from 8 months to a year before seeking medical advice. He is much more likely to be ruddy cheeked, and there are 7 to 8 chances out of 10 that he is a male, with 1 chance in 10 that he is under 40 years of age. There are 8 chances out of 10 that he will fall into the first group, those who have had no previous digestive difficulty. He is not greatly impressed with his symptoms but is much more apt to be annoyed by them. He is really not sick and may have difficulty in describing his complaint being only able to state that he has a "little stomach trouble" whose beginning he can definitely date. He is still able to play 18 holes of golf and notices that there are days when he feels quite well. His central complaint, however, is one of dyspepsia or indigestion or epigastric discomfort. He has lost that sense of well-being following a meal that was once his and its place has been taken by a consciousness of having eaten. He may complain of fullness, a smaller capacity for food, a tendency to eructate, a feeling of motion or of warmth in the epigastrium, and occasionally mild nausea. His discomfort is exactly and vividly described over the radio many times a day and recommendations for symptomatic relief are glibly given. At this time and even later relief may be obtained because these symptoms are apt to be remittent or intermittent. The distress may be intensified by food or it may be relieved by food, it may be worse as the stomach fills or as it empties. The story may exactly simulate that of gastric ulcer as to periodicity and relief by food and alkali as it did in 40 per cent of the cases studied by Jensen and Rivers. The symptoms may mimic the early story of any of the other diseases of the stomach or of any part of the gastrointestinal tract from the esophagus to the colon because early gastric cancer has no typical pattern. One should not expect pain as a symptom, however, it might be advisable to consider the epigastric discomfort, complained of so often, as a type of pain occurring in an organ *ordinarily insensitive*. If the patient falls into the second group—Friedell states that in patients under 30 over 50 per cent have had the symptoms of ulcer for an average duration

of  $4\frac{1}{2}$  years, while Walters and Walton found this history in 20 per cent—having had this previous digestive trouble, the patient will have grown familiar with its pattern. If he is sensitive he will note with the onset of more serious trouble that there has occurred a change in the degree or rhythm of his symptoms. This is an important fact in the diagnosis of gastric malignancy. Food now tends to increase the pain rather than to relieve it, and there persists a constant mild degree of nausea with occasional vomiting. One cannot, however, depend upon this change, as it may not occur. When it does the patient is apt to be more alarmed than is his physician, and herein lies a danger in that there may be some delay before the cause of the change is thoroughly investigated. The functional dyspeptic, who for years has been uncomfortable but relatively healthy, notices the onset of new and more persistent symptoms—nausea, more or less continued discomfort, and the onset of bad health in place of previous relatively good health. The patient who falls into the third group may note little digestive disturbance, but fatigue and depression are prominent. He suddenly tires easily, is less able to do his work, is more comfortable when reclining, and needs more sleep. He loses interest in his work or in his hobby and is physically unable to carry on without great effort, he has to spur himself to do what he formerly did with zest. This lack of stamina is mental as well as physical. Pernicious anemia may be thought of and treatment on that diagnosis be instituted. This progressive weakness is a prodromal sign in early cancer of the stomach and is due to metabolic changes and the products thereof which are essentially toxic and due also perhaps to some other factors of metabolic disturbance as yet unknown. Having noted these symptoms, so often mild, the sensitive patient is fortunate if he falls into the hands of a suspicious clinician, the second factor influencing the curability of his disease.

It would almost seem that physicians might be divided into two classes (1) those who are eternally *suspicious* of gastric ulcer and never find it, (2) those who are *never suspicious* of it and eternally miss it. The first are apt to complain of the futility of their efforts, and the

young patients by Friedell. Factors then which influence the curability of the disease are those which make possible the recognition and the prompt surgical treatment of the process during this stage. These factors pertain first to the patient and second to the physician and may be considered under the alliterative headings of (1) a sensitive patient (2) a suspicious clinician (3) a studious and searching roentgenologist and gastroscopist (4) a super-skillful surgeon.

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Symptoms listed by various authors include those of late as well as those present in early disease.

Gastric	Laboratory
(59 per cent, 33 of 47 resected)	(57 per cent, 30 of 53 resected)
Pain	Indigestion
1. Loss of weight	1. Anorexia
2. Vomiting	2. Pain
3. Weakness	3. Weight loss
4. Indigestion and belching	4. Vomiting
5. Loss of appetite	5. Dysphagia
6. Fullness	6. Weakness
7. Anorexia	7. Hemorrhage
8. Regurgitation	8. Constipation
	9. Diarrhea
Oughterson	10. Mucous
(58 per cent, 30 of 52 resected)	Ransom and Colfer
Abdominal discomfort	(54 per cent, 26 of 48 resected)
Loss of weight	Epigastric pain
1. Constipation	1. Anorexia
2. Eructation	2. Pain and gas
3. Anorexia	3. Pain and weakness
4. Vomiting	4. Pain and belching
5. Regurgitation	5. Nausea and vomiting
6. Diarrhea	6. Stomach trouble
	7. Dyspepsia
Harris	8. Gas
1. Gradually increasing loss of appetite	9. Abdominal distention and dyspepsia
Epigastric distress	10. Nausea and belching
2. Indistinct abdominal pain	11. Vomiting of blood
3. A history of ulcer with change in characteristics of symptoms	12. Dysphagia
4. Gradual loss of weight	13. Pain and fever
5. Gradual loss of appetite	14. Loss of weight
6. Anorexia	15. Vomiting and belching
7. A little loss of weight	16. Fainting and pain
8. Anorexia	

Most of these symptoms could be truly called those of simple dyspepsia. Those underlined are not usually due to early disease which was evidently not common in the cases upon which these lists are based, as is seen in the percentage of resectability. The prevalent idea of the symptomatology of the disease is based on more or less advanced cases. If the diagnosis is to be made while the patient is still well, as it must be if we will influence the curability, he will have to be educated to the need of being sensitive to mild degrees of gastric discomfort, and he will fall into one of three classes: (1) those who have never had digestive disturbances before, (2) those who have had previous digestive disturbance due to either organic disease or functional disturbance, or (3) those who have no digestive disturbance but rather complain of some debilitating disease. The patient who is sensitive to mild degrees of digestive discomfort is not the

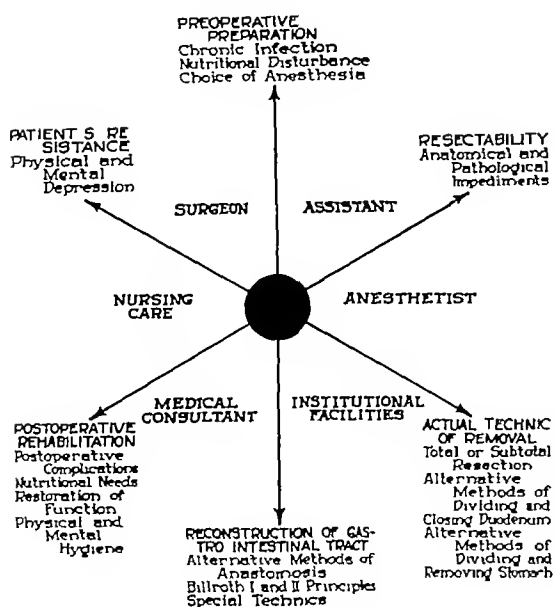


Fig 3 The surgical problem

is an evidence of ulceration of the gastro-intestinal tract, adds to the suspicion, and should be persistently traced to its source. Devine thinks that slight epigastric rigidity without deep tenderness is highly suggestive when accompanying dyspepsia. As a rule little else is found upon physical examination. If it is, the disease is usually not early and it may be that after having been as thorough as possible the clinician is left with his simple suspicion enhanced only by the added evidence of altered gastric secretion. Persisting in his search he seeks the aid of the roentgenologist and gastroscopist because it is, in the final analysis, by their efforts that the early diagnosis will be established. They must be expert, studious, searching, and persistent. With the attitude of mind that has existed in the past and still exists in many instances, the roentgenologic diagnosis of gastric carcinoma has usually been simply a confirmation of an already made clinical diagnosis and it has usually been easy and late. Christian, writing in 1924, expressed disappointment at the value of the roentgenogram in the detection of early cancer in his experience. In expert hands today it is almost 100 per cent accurate (14). In any other than expert hands it is less than useless. The failure

in roentgenographic diagnosis is largely in the case of ulcer carcinoma where after all the problem of differentiation between benign and malignant lesions in some areas of the stomach can be solved only by the pathologist (43, 12). Here the expert roentgenologist will express an opinion only on the physical characteristics of the process. The exact percentage of cancer that occurs in benign ulcer is not of great practical importance if it is appreciated that much gastric ulceration is potentially malignant and should be treated by surgical excision whenever possible. The medical test to determine the nature of an ulcer has two faults: (1) the loss of an interval of time during which the possibility of cure may cease to exist, (2) the fact that partial healing of an ulcer under medical treatment has been noted by the roentgenogram and later proved by resection to be malignant (27). In prepyloric ulcer the possibility of malignancy is so great and in ulceration of the greater curvature it is nearly always so positive that the diagnosis can be made upon the location alone. It is important to stress persistence as a virtue on the part of the roentgenologist because a patient under suspicion must not be lulled into a feeling of security by a single negative roentgenographic report. The examination must be repeated at regular intervals, preferably by the same expert. Negative roentgen-ray findings in the presence of continued symptoms, if accepted as final, may defeat the patient. It would be illuminating to know how many patients fall into the inoperable group after having had a negative roentgenographic report a short time previously. In the presence of suspicious symptoms and of negative roentgenologic findings it is pertinent for the clinician to ask the roentgenologist how he explains the symptoms. This may lead to further and more direct search elucidating the problem. Cole has demonstrated the pathological basis upon which early roentgenologic diagnosis can be made and minor but persistent defects in peristalsis due to infiltration of the submucosa by cancer cells be demonstrated. The lack of pliability he designates as the most delicate of the roentgen-ray findings. The value of many rapidly taken and superimposed films has also been demonstrated by Ledoux-Lebard who shows

second to comment on the hopelessness of the disease. That physicians lack perception and suspicion, even in their own persons, was shown by Alvarez in a study a few years ago. Fifty per cent of the physician patients studied had had symptoms for at least a year before being treated. The answers to a questionnaire which I sent out to some physicians of my acquaintance are equally revealing.

- Q Has your ever had dyspepsia or indigestion?  
 A. Often, from very many.  
 Q Has it recurred or persisted?  
 A. Often, from very many.
3. Q Have you ever taken an antacid without having had gastric analysis?  
 A. Very many had.
4. Q Have you ever had gastro-intestinal ray series on yourself?  
 A. Very few had.
5. Q Have you ever had gastric analysis?  
 A. Rarely since student days.
6. Q Do you have periodic physical examination?  
 A. Very many did so.
7. Q Do you periodically have your heart and blood pressure examined?  
 A. Very many did.
8. Q Do you periodically have your urine examined?  
 A. Very many did.
9. Q Do you consider gastro-intestinal ray series an essential part of complete physical examination?  
 A. Very few did.
- Q What are your indications for gastro-intestinal examination by the ray?  
 A. Digestive symptoms which persist in spite of adequate medical treatment. Very few considered anorexia, emaciation, fatigue or ordinary dyspepsia an indication.
- Q In what percentage of your patients do you utilize this method of diagnosis?  
 A. Many replied "in very few."
2. Q Why do you not do it in all of your patients?  
 A. Few thought it unnecessary as routine but most said it was matter of expense.

It seems obvious that a gastro-intestinal roentgenographic study is an essential part of any complete physical examination, and it is almost foolish to be content with investigating the upper and lower few inches of the gastro-intestinal tube and leaving the greater part of it unexplored. As a matter of simple precaution it would seem advisable for every physician at least to have a gastro-intestinal roentgenographic study and a gastric analysis as a part of his personal medical record. It would be interesting to know how many fellows of the American College of Surgeons harbor at the present time the benign precursors of more serious trouble. To the suspicious clinician, be

he family physician gastro-enterologist, or internist the present diagnostic methods are adequate in every way for very many more patients than those to whom they are applied. He knows that in gastric cancer it is always later than you think. He realizes that any delay in establishing a diagnosis lessens the patient's chance of having applied the only known method of cure—surgical excision. He realizes that most writers stress the need of being suspicious in the patient after 40 but he feels that it would be better to leave out this reference to age and develop the habit of thinking of gastric cancer whenever the dyspeptic syndrome is encountered. He is appalled at the number of patients who treat their own digestive trouble or who are treated without having any searching investigation of its cause, and he knows that there is no such thing as ordinary dyspepsia until it has been proved to be nothing more. Quickly aware of the serious possibilities suggested by the sensitive patient's history he makes a tentative diagnosis of carcinoma and proceeds at once to disprove it with all the methods at his command. Physical examination will probably do no more than fail to reveal any other cause for the symptoms. In 70 to 80 per cent free hydrochloric acid is low or absent, but if the acid findings in the gastric secretion are normal or above normal the suspicion will still exist in his mind. Dean Lewis considers achlorhydria to be one of the most valuable early signs, an opinion shared by Holman and Sandusky who in a recent study state that low acidity or anacidity remains the single most reliable evidence of carcinoma. Comfort, Butsch and Eusterman have shown that the acidity is practically always below normal in patients destined to develop carcinoma of the stomach and that this low acidity appears early in all ages and is persistent. Atrophic gastritis seems to be an important cause with secondary degeneration of a chronically inflamed mucous membrane often occurring. The importance of a systematic recheck of patients with achlorhydria and the need of continued suspicion in such cases are imperative. Occult blood in the gastric content and stool is rare in early carcinoma, appearing more constantly in the latter when the disease is further advanced than it

resistance, (2) institution of methods to increase that resistance and safeguard the patient, (3) decision as to the resectability of the tumor, (4) the actual resection of the tumor, (5) the re-establishment of the gastro-intestinal tract, (6) the mental and physical rehabilitation of the patient after operation. The most effective answer to this question demands a wisdom and a knowledge founded upon the widest experience, and to choose the surgeon upon any other basis is to make a grievous and fundamental error. The experienced surgeon knows what he can do, the inexperienced frequently misjudges his capacity. The experienced will consider lesions as resectable in patients who have been refused operation in less experienced hands, and he will be able to carry it to a successful conclusion. Consequently, he who attempts this type of surgery must measure his abilities against the highest standard, and no one should attempt to operate upon a patient with gastric cancer unless he is qualified and intends to resect the growth in the most radical manner. He should be willing to undertake to do this on the basis of expert roentgenologic and gastroscopic opinion alone, realizing that in early cases even the most experienced may be unable to demonstrate any gross pathology by palpation or visualization. Numerous instances have been reported in which the possibility of roentgen-ray diagnosis was demonstrated at a time when the lesion was macroscopically undemonstrable (15).

TABLE I—RESECTABILITY AND OPERATIVE MORTALITY—RECENT AMERICAN CONTRIBUTIONS

	Total Cases	Resections Per cent	Mortality Per cent
Gray and Balfour	4773	1050, 22.6	13.03
St. John, Whipple, Raiford	718	98, 13.6	37.7
Lewisohn, Mage	647	93, 14.3	33
Gatewood	417	58, 13.9	32.6
Ransom, Collier	415	56, 13.4	23.2
Lahey	195	50, 25.7	35
Parsons and Welsch	691	171, 25	
MacC, Boyce, and McFetridge	758	35, 4.6	51.4
Oughterson	120	19, 15.8	52.6
Maxeiner	60	18, 30	16
Minnes and Geschickter	541		
Pack and Livingston	229	26, 11	11.4
Abrahamson and Hinton	444	24, 5.4	58.3

The experienced surgeon will have in mind primarily the complete removal of the disease

and not some preconceived plan of restoring the gastro-intestinal tract. He will, rather, be in command of all of the methods available for restoration and will be able to decide upon and to apply the proper one after removal of the growth, no matter in what condition it has left the gastro-intestinal tract. But to do this he will need great resource and skill and, above all, flexibility of technique. These are qualities which come only with extensive experience so that this type of surgery is not for the occasional operator, the general practitioner surgeon, or the inexperienced. Since it is not given to all surgeons to see many cases of gastric carcinoma or to have the opportunity of operating upon a large series, it is quite imperative that these cases fall into properly trained and competent hands. However, even the greatest skill cannot overcome the handicap of advanced and disseminated disease. The difficulties inherent in the location of some cancers of the stomach are gradually being overcome with perfection of technique. Walters has recently reported only 14.7 per cent mortality in 34 cases of carcinoma at the cardia, and a combined thoraco-abdominal approach may make possible the successful resection of more growths in this area. To stress technique as a cause and statistical evidence of results as the justification of success is not always warranted. However, the study of mortality figures remains the best method of appraisal. The average operative mortality is in the neighborhood of 25 per cent. A select group of surgeons account for one-third of all the resections reported in the last 20 years with an operative mortality of less than 10 per cent. Christopher states that in "skilled hands" the mortality should be less than 15 per cent. That this qualifying phrase does not cover the casual surgeon is shown by the fact that his operative mortality is twice as high as that of the surgeon who is constantly occupied with this problem. This has been conclusively shown by Pack and Livingston who confirm a previous report by Verbrycke on the mortality of the casual surgeon in another and even less difficult field. Ablative surgery is, after all, a crude method of treating this disease but it remains a fact that it is the only successful method so far at hand. Keynes speaking on



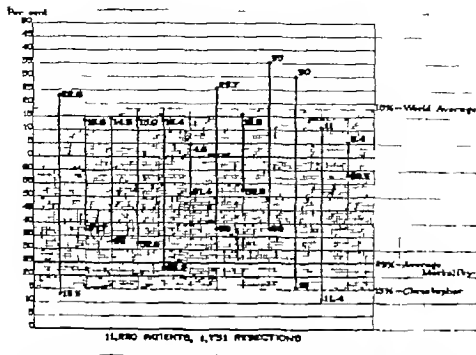


Fig. 4. Relation of operative mortality to resectability. Reports from recent American contributions. Upper figures represent resectability. Lower figures represent operative mortality. Vertical lines connect figures from same series. Shaded area is below the range of resectability and above the average of operative mortality.

their value in the detection of obliteration of the rugae, changes in the mucosal pattern and persistent defects in peristalsis. Gross filling defects due to ulceration or tumor are not due to early disease. The quality of the roentgenogram taken regardless of expense is of the most vital importance to the patient. The question of expense should not be considered when the need and possibilities of benefit are weighing in the balance. In the event of equivocal or doubtful findings by the roentgen-ray or when they are completely negative in suspicious cases, the stomach should be directly inspected by an experienced gastroscopist. Occasionally gastroscopy gives evidence not obtained by any other method and it should be a part of the routine study of the stomach. Its greatest value is in the differential diagnosis of benign and malignant ulcer according to Balfour but early cancer may be detected during a routine examination. In all cases of achlorhydria it would be valuable to inspect the interior of the stomach and to record the appearance of the

mucous membrane for future information, repeating the examination every 6 months to a year. It is in combination with the roentgen-ray however and as an adjunct to it that gastroscopy is most useful and its value is again directly proportionate to the skill and the experience of its user. It is not, however, absolutely dependable when taken alone but when its positive evidence is added to doubtful roentgenographic evidence it is of the greatest value.

Having added to the suspicions of the clinician the evidence of the roentgenogram and the gastroscopy there remains that last factor in the cure of the patient with gastric cancer that is, the *superskillful surgeon*. There is probably no other condition in abdominal surgery that demands as high a degree of skill and as wide an experience as does the surgery of gastric cancer. It is here that art and science meet in method. The problem presented to the surgeon is manifold and comprises many elements: (1) An estimation of the patient's

# SULFONAMIDE THERAPY AS AN AID TO SURGERY

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IN this paper an attempt will be made to focus on the problems of surgical infections the knowledge which has been gained through study of the mode of action and the therapeutic limits of the sulfonamide compounds. The term "sulfonamides" is employed to include the three drugs in greatest current use, sulfanilamide, sulfapyridine, and sulfathiazole. I shall not discuss many important details concerning dosage, toxicity, and selection of drugs, for these points are adequately covered in numerous papers in the current literature (2, 8, 12, 17), but I hope to outline the general principles underlying the successful use of the sulfonamide compounds in surgical infections, and to present, very briefly, a hypothesis of the mechanism of the action of sulfonamide compounds which I believe is in conformity with most of the available experimental and clinical data. This hypothesis supplies a theoretical framework upon which a complete scheme of sulfonamide chemotherapy may be constructed.

## A WORKING HYPOTHESIS OF THE MODE OF ACTION OF SULFONAMIDE COMPOUNDS

Bacteria produce the pathological processes of infection by reason of their capacity to become parasites in the body. As is the case with all parasites, they obtain their "food" requirements by altering the constituents of the body tissues to suit their own particular needs. Bacteria cannot make direct use of large unsplit molecules of protein. The protein molecules of the host must first be broken down into the simpler component amino-acids or polypeptides through the activity of a large number of enzymes, each enzyme being responsible for a certain link in the chemical chain of events. The enzyme completes the particular chemical reaction which it is designed to facilitate when it becomes coupled

with the appropriate molecule in its environment. The enzymes must all work together as a team if the supply of energy is to be maintained and if the building stones of new generations of bacteria are to be shaped and fitted together successfully. Failure of any one of the essential enzymes to perform its function properly will disrupt the entire mechanism of bacterial reproduction. It is here that the sulfonamide compounds produce their effects. These compounds bear a close resemblance to certain chemical substances which are essential to bacterial nutrition, of which one, at least, appears to be p-aminobenzoic acid (19) (Fig. 1). Figure 2 shows diagrammatically

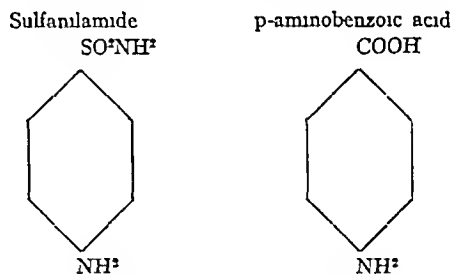


Fig. 1 Structural formulas of sulfanilamide and p amino benzoic acid

how molecules of sulfanilamide may cover up the particular point of molecular reactivity on the bacterial surface, or enzyme, and thereby prevent the proper coupling of p-amino benzoic acid to this enzyme. The effect of this process, called "competitive enzyme inhibition" by the biochemists, is to prevent bacterial utilization of p-aminobenzoic acid, with the result that the cell ceases to divide. Such interference with bacterial reproduction may be termed "bacteriostasis." If there are present on the bacterial surfaces a very large number of enzymes capable of utilizing p-aminobenzoic acid, or if there is an excess of p-aminobenzoic acid in the environment, the number of sulfonamide molecules required to block all of the enzymes and to stop bacterial growth altogether will necessarily be correspondingly

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the future of surgery prophesied that cancer will eventually be treated by the intravenous injection of a specific. The temptation is great in the face of such a complex problem to build up a hypothesis and to assume that it is an expression of reality. It is more important to cast aside meaningless and useless doubts and to dispel the air of pessimism that exists by attempting more thoroughly and skillfully to utilize what is known until better information is available. In our efforts to use all the factors for success we must create both in the patient and in the physician an appreciation of the dangers of mild digestive symptoms. We must then see that these patients are investigated thoroughly repeatedly and expertly and finally that in treatment only the most expert surgery is offered to them. In the war against this dread and sinister disease it may be that our efforts are simply skirmishes on the margin of the battle, but even if it be so they must be fought with every means at our command and they call for our utmost vigilance and our most persistent effort.

## BIBLIOGRAPHY

- ABRAHAMSON, R. H. and HINTON, J. W. Carcinoma of the stomach. *Surg. Gynec. & Obst.*, 1919, 7, 25.
- ALBRECHT, W. C. How early do physicians diagnose cancer in themselves? *J. Am. M. Ass.*, 1931, 97, 77.
- BALFOUR, D. C. Curability of cancer of the stomach. *Surg. Gynec. & Obst.*, 1934, 58, 313.
- Idem. The place of the gastroscope in the diagnosis of lesions of the stomach and the duodenum. *Arch. Surg.*, 1940, 4.
- CHRISTIAN, H. A. Some observations, largely pessimistic on the early diagnosis of gastric carcinoma. *J. Am. M. Ass.*, 1934, 8, 30.
- CROFTON, FREDERICK. Carcinoma of the stomach. I. *Internat. Abstr. Surg.*, 1930, 63, 57.
- COLE, LAWRENCE GREGOR. Gastric cancer: correlation of roentgenological and pathological findings. *Am. J. Surg.*, 1936, 3, 300.
- CONROD, M. L., BUTCHER, R. L. and ECKHART, V. O. B. Observations on gastric acidity before and after development of carcinoma of the stomach. *Am. J. Digest. Dis.*, 1937, 4, 673.
- COOK, J. W. Discussion on experimental production of tumors. *Proc. Roy. Soc.*, 1935, 3, 273.
- DEVANEY, See HIGGS. *Surgery of the Alimentary Tract*. Baltimore: Williams & Wilkins Co., 1940.
- DODDS, E. C. The hormones and their chemical relations. *Lancet*, 1934, 70, 91, 957, 943.
- FRIEDBERG, H. Malignant degeneration of gastric ulcer. *Proc. Roy. Soc. Med.*, 1930, 3, 83.
- FRIEDBERG, M. T. Prolonged history of carcinoma of the stomach in persons in the third decade of life. *Proc. Staff Meet. Mayo Clin.*, 1939, 4, 520.
- GREGG, OOO. Carcinoma of the stomach. An analytical survey. *T. Am. Surg. Ass.*, 1934, 30, 108.
- GONNETT, A., GUTTEN, R. A. and BERTHAUD, The diagnosis of beginning cancer. *Bull. et mém. Soc. mé. d. hôp. de Par.*, 1923, 41, 5, 2.
- GRAY, H. K. and BALFOUR, D. C. Cancer of the stomach. *Am. J. Cancer*, 1934, 440.
- HARRIS, S. ALF. Early symptomatology and diagnosis of gastric cancer. *Am. J. Surg.*, 1930, 3, 5.
- HOGAN, C. W. and SANDERBY, W. R. Further observations in the diagnosis and treatment of gastric lesions. *Ann. Surg.*, 1940, 139.
- JEWETT, R. M., RIVERA, A. B. Carcinoma or ulcer in obliterating the pyloric ring. *Proc. Staff Meet. May Clin.*, 1930, 14.
- KEVES, GEORGE. Malignancy, or the letters of surgery. *Lancet*, 1934, 70, 943.
- LARRY, FRANK H. Cancer of the stomach. *Surg. Gynec. & Obst.*, 1935, 6, 246.
- LINDORF, LUDWIG, R. Advances in the treatment of gastric cancer. *Brit. J. Radiol.*, 1940, 3, 37.
- LININ, DEAN. Carcinoma of the stomach. *Practitioner*, 1931, 3, 250.
- LEWIS, R. and SMITH, S. Five year cases of cancer of the stomach. *Surg. Gynec. & Obst.*, 1935, 60, 457.
- MCCARTHY, W. C. Cancer of the stomach. *Radiol. Surg.*, 1940, 34, 1.
- MAY, BOYCE and MCFARLANE. The tragedy of gastric carcinoma. *Ann. Surg.*, 1935, 60, 6.
- MALLORY, TRACY B. Carcinoma in situ of the stomach and its bearing on the histogenesis of malignant ulcers. *Arch. Path.*, 1940, 30, 343.
- MALMSTEDT, S. R. Carcinoma of the stomach. *Minnesota Med.*, 1935, 8, 484.
- MORLEY, J. T. and GARDNER, C. T. Some clinical features of carcinoma of the stomach. *Am. J. Cancer*, 1936, 27, 740.
- NICHOLSON, J. Substances promoting normal and abnormal growth. *Brit. M. J.*, 1935, 701.
- ONCARTER, A. W. End results in treatment of cancer of stomach. *Yale J. Biol. & Med.*, 1935, 41, 713.
- OWENS, NEAL. Cancer. *New Orleans M. & S. J.*, 1938, 30, 354.
- PACE and LEVINTHAL. End Results in the Treatment of Gastric Cancer. New York: Paul B. Hoeber Inc., 1930.
- PALBOUR, L. and WELSH, C. E. Curability of gastric cancer. *Surgery*, 1938, 6, 127.
- R. VON, H. K. and COLLIER, F. A. Carcinoma of the stomach: observations on the surgical treatment. *J. Michigan State M. Soc.*, 1935, 3, 87.
- RIVERA, ANDREW B. The importance of cancer as a cause of chronic dyspepsia. *J. Am. M. Ass.*, 1939, 3, 88.
- ST. JOHN, F. B., WHIFFLE, A. D. and RAYBOLD, T. S. Treatment of carcinoma of the stomach. *Am. J. Surg.*, 1935, 3, 245.
- SALTZSTEIN, H. C. and SANDWICH, D. J. The problem of cancer of the stomach. *Arch. Surg.*, 1939, 3.
- VALENTINE, J. R. Gall bladder operative mortality. *South M. J.*, 1936, 452.
- WALTER, WALTER. Cardiac gastric ulcers. *Arch. Surg.*, 1940, 4, 542.
- WATSON, J. Carcinoma of the stomach. *Brit. M. J.*, 1930, 3, 37.
- WARREN, S. Analysis of one hundred seventy-six cases of carcinoma of the stomach submitted to autopsy. *Ann. Surg.*, 1938, 108, 6.
- WELLS, W. L. A. Early gastric cancer. *Arch. Path.*, 1939, 8, 735.

nilamide powder in wounds, as reported by Jensen, Johnsrud, and Nelson, is probably a result of the very high local concentration so obtained, a concentration which might be expected to inhibit the growth of almost any type of contaminating bacteria. The local implantation of crystalline sulfonamide compounds into suppurative lesions which have been opened and drained deserves investigation as a possible means of supplementing the limited effectiveness of these drugs in such lesions when they are administered by the systemic routes (17). Furthermore, one should select for treatment in any given case a drug which can be transported to the infected region in adequate concentration. For example, the recent observation by Carey of the limited absorption of sulfathiazole into the spinal fluid is perhaps a contra-indication to the use of this drug in the treatment of meningitis, and suggests the advisability of using sulfapyridine in the treatment of suppurative infections of the meninges. A drug which is highly effective *in vitro* against most of the bacterial species but which is not efficiently transported to serous cavities will perhaps be of less therapeutic value in peritonitis than another drug, having a lower bacteriostatic power but transported in high concentration to the infected area. In the treatment of peritonitis, one should hesitate to substitute a new drug for sulfanilamide until convincing evidence is at hand of the superiority of the new drug within the peritoneum as well as in the test tube. Future progress in chemotherapy may follow the line of developing compounds which will be of value not for any greater specific effect on individual species of bacteria but rather because of special properties of absorption and distribution which cause them to attain high concentrations in infections of certain pathological types or anatomical locations. As an example of progress along this line, Marshall has recently described a new compound (14), sulfanilylguanadine, which is poorly absorbed from the gastro-intestinal tract, but nevertheless is soluble and builds up very high concentrations in intestinal secretions and feces. He reports the occurrence of a very striking reduction in the numbers of *Escherichia coli* in the intestinal tract follow-

ing its ingestion. A drug of this type might, as suggested by Marshall, be of especial usefulness in the treatment of enteric infections or in the prevention of peritonitis after colon resections.

2 *The mobilization of the cellular defense* The anatomical location of an infection, with particular respect to the capacity of the phagocytic defense in the area, is another factor which will tend to modify the magnitude of the curative effect of sulfonamide compounds. The highly developed cellular defense of the peritoneum is probably an important factor in the successful application of sulfonamide therapy in the prevention and treatment of peritonitis due to intestinal bacteria (4, 11, 16). Types of bacteria which are relatively resistant in the test tube to the bacteriostatic action of sulfanilamide are apparently affected by the drug within the peritoneum, at least they appear to be attenuated sufficiently to render them susceptible to destruction by the phagocytes with which peritoneal surfaces and exudates are richly supplied. The *Clostridium welchii* produces a fatal infection in the peritoneum of the mouse or the rabbit but death can be prevented by sulfonamide therapy (1). However, if the same organism is injected intramuscularly, the drug is quite ineffective (7, 18), and the course of the infection continues to death of the animal. The intestinal streptococci which Meleney believes (15) occur very frequently in symbiosis with *Escherichia coli* as pathogens in peritonitis of intestinal origin are relatively resistant to the effects of sulfonamide compounds—but our clinical studies suggest that sulfonamide therapy is probably of great value in the prevention and treatment of this disease in humans (11, 16).

3 *The concentration of sulfonamide inhibitor substances* The final factor of importance in conditioning the curative action of sulfonamide in infections is the amount of "sulfonamide inhibitor" in the infected area. Invasive infections caused by hemolytic streptococci tend in their early stages to spread rapidly through tissues without actually causing necrosis in the infected area. Necrosis develops later if the individual survives long enough to bring about an effort at localization

great. The concentration of sulfonamide required for complete bacteriostasis may be greater than is supplied to the area through the physiological process of drug transport. However, if the molecules of sulfonamide greatly outnumber the molecules of p-aminobenzoic acid the bacteria cease to multiply, their toxin production stops, and they will die either from "starvation" or by falling prey to the phagocytic cells of the host. When this sequence takes place in the body, the infection no longer spreads into new areas, the bacteria are destroyed, and the patient recovers.

P-aminobenzoic acid is one of a group of substances which perhaps have in common some characteristic chemical configuration, and which act as inhibitors of sulfonamide bacteriostasis. Fildes (3) believes that they are probably "intermediary metabolites" which are essential to the bacteria at some stage in their growth cycle. Sulfonamide inhibitors are present also in peptone (10) and apparently in most enzymatic digests of protein. Pus and necrotic tissue contain large amounts of sulfonamide inhibitors (13). The sulfonamide inhibitors are apparently bound up in the tissue proteins, and are neither available for bacterial utilization nor capable of inhibiting sulfonamide until released through enzymatic degradation of protein. Bacteria which have the capacity of digesting tissue rapidly such as staphylococci, or bacteria which are in pus or necrotic tissue, are so richly supplied with "sulfonamide inhibitor" substances that they are resistant to the concentrations of sulfonamide compounds ordinarily obtainable within an area of inflammation. There is evidence to indicate that sulfapyridine and sulfathiazole are more effective than sulfanilamide *in vitro* because of the larger amounts of sulfonamide inhibitor required to overcome their bacteriostatic effects. An explanation of the supremacy of sulfapyridine and of sulfathiazole over sulfanilamide in staphylococcal infections is thus provided by the work of Woods (19) who showed that it takes five times as much p-aminobenzoic acid to inhibit sulfapyridine action *in vitro* as it takes to inhibit sulfanilamide.

This hypothesis explains the importance of maintaining uniform effective levels of sulfo-

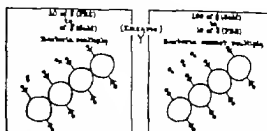


Fig. 2. Diagrammatic representation of competition for enzyme between sulfanilamide and p-aminobenzoic acid.

namide in any patient under treatment by administering the drug at four hourly intervals it accounts for differences in the susceptibility of different types of bacteria. It supplies the reason for the great effectiveness of sulfonamide compounds in the treatment of the early stages of acute pleuritis and peritonitis (regardless of the bacterial species involved) and finally it clarifies the importance of combining timely surgical interference with chemotherapy in the management of many different types of infections. The three principal factors which will tend therefore, to modify the magnitude of the curative effect of sulfonamide compounds in infections may be listed as follows:

1. The concentration of the drug maintained in the immediate environment of the bacteria. In some lesions, as in erysipelas, for example, the concentration of drug required to bring about death of all the streptococci appears to be fairly low, perhaps only 1 or 2 milligrams per 100 cubic centimeters. However, in lesions characterized by early necrosis, and the consequent liberation of inhibitor substances, such as in staphylococcal cellulitis, a concentration of even 15 to 20 milligrams per 100 cubic centimeters may succeed only in restricting the spread of the infection to new areas. It is particularly important therefore, in staphylococcal infections to maintain as high a level of sulfonamide as is compatible with toxic limitations. The amount of drug required for successful treatment of urinary tract infections, due to *Escherichia coli*, is not great, because sulfonamides are excreted by the kidneys in active form and are present in very high concentration in the urine (5). The prophylactic value of local implantation of sulfa-

treatment, so that any foci of localization may develop clinical evidence of their existence. Drug treatment should then be resumed in conjunction with the surgical treatment of these abscesses.

This last factor, involving the amount of sulfonamide inhibitor, appears to me to be the most important of the three which we have discussed. This may be translated into clinical reality in any given case by asking oneself the following question: "How much actual necrosis and digestion of tissue is taking place in this infection?" If the infection may be pictured as a diffuse one, in which the blood supply of the entire infected zone is intact, then one may anticipate a satisfactory result from chemotherapy alone. However, the surgeon must be prepared to remove the gangrenous appendix, or drain the necrotic mastoid, or evacuate the empyema pocket when these or similar complications appear to be present, as the drug alone will not cure these lesions and may serve to endanger the patient through masking their existence.

The chronically draining sinuses which sometimes persist following a suppurative lymphadenitis due to hemolytic streptococci appear to respond well to sulfanilamide therapy alone. (9) The rapid disappearance of the organisms from the exudate after institution of drug treatment is probably a result of the fact that this particular exudate does not contain products of continuing tissue digestion, but is composed chiefly of the lymph which bathes the infected area. After the streptococci disappear, the sinuses tend rapidly to close. In chronic infections of this type, particularly those in which the hemolytic streptococcus is present in pure culture, it is advisable to try the effect of a course of sulfanilamide before radical surgery is resorted to. Less should be expected of chemotherapy, however, in the treatment of the chronic suppurative complications of staphylococcal infections.

Many of the principles outlined in this paper are shown in abbreviated form in the accompanying table (Table I). The classification of infections, according to the 5 stages shown, is admittedly only an approximation and some of the rules suggested may need to be changed in the light of further experience.

## SUMMARY

1 Sulfonamide compounds produce their effects in infectious lesions by exercising a bacteriostatic effect on the organisms.

2 This bacteriostatic effect is probably a result of a specific interference with the enzymatic utilization by the bacteria of some nutritive chemical factor, such as p-aminobenzoic acid.

3 These substances, the utilization of which is blocked by sulfonamide, will act as inhibitors of sulfonamide effects when they are present in more than minimal concentrations.

4 The curative effects of sulfonamides are maximal when the concentration of the drug is high, when the local cellular defense is active, and when the concentration of sulfonamide inhibitors in the infected area is low.

5 Localized areas of tissue necrosis and abscesses contain large quantities of sulfonamide inhibitor. The organisms within such lesions are protected against the effects of sulfonamides.

6 Surgical treatment of sulfonamide-resistant lesions is of great importance.

## BIBLIOGRAPHY

- 1 BLISS, E. A., FEINSTONE, W. H., GARRETT, A. W., and LONG, P. H. *Proc Soc Exper Biol*, 1939, 40 619
- 2 CAREY, B. W. *J Am M Ass*, 1940, 115 924
- 3 FILDES, P. *Lancet*, 1940, 1 955
- 4 GARLOCK, J. H., and SELEY, G. P. Preliminary report. *Surgery*, 1939, 5 787
- 5 HELMHOLTZ, H. I. *Proc Staff Meet Mayo Clin*, 1940, 15 65
- 6 JENSEN, N. K., JOHNSRUD, L. W., and NELSON, M. C. *Surgery*, 1939, 6 1
- 7 KENDRICK, D. B., JR. *J Clin Invest*, 1939, 18 593
- 8 LOCKWOOD, J. S. *J Am M Ass*, 1940, 115 1190
- 9 LOCKWOOD, J. S., COBURN, A. E., and STOKINGER, H. E. *J Am M Ass*, 1938, 111 2259
- 10 LOCKWOOD, J. S., and LYNCH, H. M. *J Am M Ass*, 1940, 114 935
- 11 LOCKWOOD, J. S., and RAVDIN, I. S. *Surgery*, 1940, 8 43
- 12 LONG, P. H., HAVILAND, J. W., EDWARDS, L. B., and BLISS, E. A. *J Am M Ass*, 1940, 115 364
- 13 MACLEOD, C. J. *Exper Med*, 1940, 72 217
- 14 MARSHALL, E. K., JR., BRATTON, A. C., WHITE, H. J., and LITCHFIELD, J. T., JR. *Bull Johns Hopkins Hosp*, 1940, 67 163
- 15 MELENEY, F. L., OLPP, J., HARVEY, H. D., and JERN, H. Z. *Arch Surg*, 1932, 25 709
- 16 RAVDIN, I. S., RHOADS, J. E., and LOCKWOOD, J. S. *Ann Surg*, 1940, 111 53
- 17 SPINK, W. W., and HANSEN, A. E. *J Am M Ass*, 1940, 115 840
- 18 STEPHENSON, D., and ROSS, H. E. *Brit. M J*, 1940, 1 471
- 19 WOODS, D. D. *Brit. J Exp Path*, 1940, 21 74

TABLE I—EFFECTIVENESS OF SULFONAMIDE IN RELATION TO THE ADJUSTMENT OF FACTORS MODIFYING ITS BACTERIOSTATIC PROPERTIES IN INFECTIONS AT VARIOUS STAGES OF DEVELOPMENT

Stages	Adjustment of factors influencing effectiveness of sulfonamide			Direct effectiveness of sulfonamide treatment	Duration of sulfonamide treatment	Other therapeutic considerations
	Concentration	Phagocytosis	Antibiotic factors			
I Contaminated wound, otitis, traumatic cilia reaction, leukorrhea	++ to ++++ (local)	Varies with location	Varies with amount of dermal infection	Maximal (interfered with thrombolytic factors)	Prophylactic treatment for 3-5 days Primary implication of epithelial sulfonamide	Avoidance of unnecessary trauma. Thorough debridement and irrigation of contaminated wound.
II Invasive infection, erysipelas, cellulitis, lymphangitis, streptococcal hemolytic septicaemia, acute pyelitis, acute cystitis, pneumonia, septic proctitis	++ to +++	Varies with site and depth	Low	Maximal	Continued until 3-4 days after subsidence of infection	Avoidance of surgical intervention. Extensive debridement and wet dressings to infective part. Administration of specific antibiotic if available. Control supportive treatment.
III Invasive infection, plus localized abscess, staphylococcal infection, streptococcal infection, suppurative parotitis, paronychia, paronychia	++ to +++	Varies with severity and location	Peripheral—low Central—high	Maximal at periphery of wound within zone of infection	Continued at least 10-12 days after surgical drainage of the localized area	Drainage or removal of localized area of infection after clearing sulfonamide treatment. Other considerations as in II.
IV Localized abscess, carbuncle, suppurative paronychia, paronychia, chronic staphylococcal infection	++ to +++	Localized	High	Maximal	Drug treatment only as adjunct of surgical drainage. Hypertonic local applications	Drainage or removal of localized abscess.
V Chronic non-suppurative infection, pyelitis, chronic cystitis, chronic leukorrhea, chronic leukorrhea	++ to ++++ (local)	Periodically active	Low to moderate	Intermittent to maximal	Continued for weeks or longer (Prophylactic treatment may be necessary in pyelitis)	Surgical intervention only if local infection persists in chronic phase which may need debridement. (Note: agents for local application may be necessary in case infection with sulfonamide)

of the infection. However necrosis of tissue may develop fairly early in the course of staphylococcal infections, due in part to the production of proteolytic enzymes by this organism. Fortunately the sulfonamide compounds produce their most striking effects in the early invasive stages of these infections, at a time when surgical intervention is of little value. The amount of sulfonamide inhibitor in newly infected tissue or in the blood stream and lymphatics is apparently not great, so that maximal bacteriostatic action of the drug is obtained. After localization and necrosis have occurred, the sulfonamide inhibitors are released, and the sulfonamide has little effect on the suppurative component of the infection, at least when it is administered through the systemic route. Here surgical drainage is of paramount importance. If the abscess is removed or is opened and drained, then the sulfonamide may exercise a bacteriostatic effect on the organisms left in the intact

periphery of the lesion, or in the lymph which bathes the wound after necrosis is completed, and final healing may be hastened. In my experience the recovery of patients with staphylococcal septicemia and meningitis has rarely occurred with intensive chemotherapy alone. It is of great importance and contributes largely to the final recovery if possible suppurative foci of localization are attacked surgically without great delay. Patients with staphylococcal septicemia may frequently respond very favorably after 2 or 3 days of intensive treatment with sulfathiazole—their blood cultures may become sterile and they may appear to be well on the road to recovery. However almost invariably the prolonged continuation of chemotherapy serves only to mask the presence of small localized abscesses which will continue as foci of toxic absorption until they are drained surgically. It now seems to me to be preferable to stop the drug in such cases after about 10 to 14 days of

treatment, so that any foci of localization may develop clinical evidence of their existence. Drug treatment should then be resumed in conjunction with the surgical treatment of these abscesses.

This last factor, involving the amount of sulfonamide inhibitor, appears to me to be the most important of the three which we have discussed. This may be translated into clinical reality in any given case by asking oneself the following question: "How much actual necrosis and digestion of tissue is taking place in this infection?" If the infection may be pictured as a diffuse one, in which the blood supply of the entire infected zone is intact, then one may anticipate a satisfactory result from chemotherapy alone. However, the surgeon must be prepared to remove the gangrenous appendix, or drain the necrotic mastoid, or evacuate the empyema pocket when these or similar complications appear to be present, as the drug alone will not cure these lesions and may serve to endanger the patient through masking their existence.

The chronically draining sinuses which sometimes persist following a suppurative lymphadenitis due to hemolytic streptococci appear to respond well to sulfanilamide therapy alone. (9) The rapid disappearance of the organisms from the exudate after institution of drug treatment is probably a result of the fact that this particular exudate does not contain products of continuing tissue digestion, but is composed chiefly of the lymph which bathes the infected area. After the streptococci disappear, the sinuses tend rapidly to close. In chronic infections of this type, particularly those in which the hemolytic streptococcus is present in pure culture, it is advisable to try the effect of a course of sulfanilamide before radical surgery is resorted to. Less should be expected of chemotherapy, however, in the treatment of the chronic suppurative complications of staphylococcal infections.

Many of the principles outlined in this paper are shown in abbreviated form in the accompanying table (Table I). The classification of infections, according to the 5 stages shown, is admittedly only an approximation and some of the rules suggested may need to be changed in the light of further experience.

## SUMMARY

1 Sulfonamide compounds produce their effects in infectious lesions by exercising a bacteriostatic effect on the organisms.

2 This bacteriostatic effect is probably a result of a specific interference with the enzymatic utilization by the bacteria of some nutritive chemical factor, such as p-aminobenzoic acid.

3 These substances, the utilization of which is blocked by sulfonamide, will act as inhibitors of sulfonamide effects when they are present in more than minimal concentrations.

4 The curative effects of sulfonamides are maximal when the concentration of the drug is high, when the local cellular defense is active, and when the concentration of sulfonamide inhibitors in the infected area is low.

5 Localized areas of tissue necrosis and abscesses contain large quantities of sulfonamide inhibitor. The organisms within such lesions are protected against the effects of sulfonamides.

6 Surgical treatment of sulfonamide-resistant lesions is of great importance.

## BIBLIOGRAPHY

- 1 BLISS, L. A., FEINSTONE, W. H., GARRETT, A. W., and LONG, P. H. *Proc Soc Exper Biol*, 1939, 40 619.
- 2 CAREY, B. W. *J Am M Ass*, 1940, 115 924.
- 3 FILDES, P. *Lancet*, 1940, 1 955.
- 4 GARLOCK, J. H., and SELEY, G. P. Preliminary report. *Surgery*, 1939, 5 787.
- 5 HELMHOLTZ, H. F. *Proc Staff Meet Mayo Clin*, 1940, 15 65.
- 6 JENSEN, N. K., JOHNSRUD, L. W., and NELSON, M. C. *Surgery*, 1939, 6 1.
- 7 KENDRICK, D. B., JR. *J Clin Invest*, 1939, 18 593.
- 8 LOCKWOOD, J. S. *J Am M Ass*, 1940, 115 1190.
- 9 LOCKWOOD, J. S., COBURN, A. E., and STOKINGER, H. E. *J Am M Ass*, 1938, 111 2259.
- 10 LOCKWOOD, J. S., and LYNCH, H. M. *J Am M Ass*, 1940, 114 935.
- 11 LOCKWOOD, J. S., and RAVDIN, I. S. *Surgery*, 1940, 8 43.
- 12 LONG, P. H., HAVILAND, J. W., EDWARDS, L. B., and BLISS, E. A. *J Am M Ass*, 1940, 115 364.
- 13 MACLEOD, C. *J Exper Med*, 1940, 72 217.
- 14 MARSHALL, E. K., JR., BRATTON, A. C., WHITE, H. J., and LITCHFIELD, J. T., JR. *Bull Johns Hopkins Hosp*, 1940, 67 163.
- 15 MELENFY, F. L., OLPP, J., HARVEY, H. D., and JERN, H. Z. *Arch Surg*, 1932, 25 709.
- 16 RAVDIN, I. S., RHOADS, J. E., and LOCKWOOD, J. S. *Ann Surg*, 1940, 111 53.
- 17 SPINK, W. W., and HANSEN, A. E. *J Am M Ass*, 1940, 115 840.
- 18 STEPHENSON, D., and ROSS, H. E. *Brit M J*, 1940, 1 471.
- 19 WOODS, D. D. *Brit J Exp Path*, 1940, 21 74.



## RECENT PROGRESS IN THE SURGICAL TREATMENT OF CARCINOMA OF THE ESOPHAGUS

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PROGRESS in the surgical treatment of carcinoma of the esophagus has not kept pace with that of other thoracic tumors. Torek's (15) successful resection of the thoracic esophagus in 1913 gave rise to considerable interest and hope in the management of this lesion. However in spite of an abundance of investigative work and many attempts by a large number of surgeons to repeat Torek's accomplishment, only 14 successful resections were reported up to 1934 (3) all of which expired of metastases within 2 years following operation.<sup>1</sup>

This almost uniform failure to respond to therapeutic measures had been due chiefly to three factors (1) lack of early correct diagnosis (often inexcusable) (2) late development of principles of intrathoracic surgery and (3) poor response to radiation therapy. The first two of these factors are influenced fundamentally by the pathological characteristics of the tumor.

The onset of the lesion is very insidious, the condition frequently being far advanced before symptoms become manifest. These are usually very mild when first noted and little attention is given them by either the patient or the physician. They may be brought about by the (1) mechanical obstruction of the passageway by the tumor (2) influence of the tumor on adjacent structures or by (3) metastatic lesions.

Although not typical for this condition dysphagia is the first and most outstanding symptom in the majority of cases. The location of the tumor signifies little in this respect except in the interval between the act of swallowing and the experiencing of a sense of obstruction. By far the majority of the tumors are located in the middle and lower seg-

ments of the esophagus, only approximately 10 per cent arising in the upper portion.

Due to its close proximity to other important structures complications caused by direct extension of the tumor are common (about 50 per cent). The first symptoms noted may be from this source a fact which partially accounts for the variability of the clinical course. The structures most frequently involved include lung parenchyma, trachea, primary bronchi, pleura, pericardium, blood vessels and nerves (1).

In addition to the direct influence of the tumor on the wall of the esophagus and neighboring structures, metastases by way of the lymph and blood stream are of primary importance in both diagnosis and treatment. Extension of the tumor in this manner is quite variable. Dormann's reported distance metastases in about 60 per cent of a large series of 1679 collected cases. Occasionally metastases are widespread and give rise to symptoms before any evidence of the primary growth is manifested.

Spread by way of the lymphatics is most frequent, the lymph flow of the upper two-thirds of the organ being toward the mediastinal bronchial, and supraclavicular lymph glands, while that of the lower esophagus is directed toward the cardiac glands along the lesser curvature of the stomach. Distant metastases have been reported in almost every organ or structure in the body.

Real progress in the development of intrathoracic surgery has been made only in the past two decades. Prior to this time, alteration of the physiology of thoracic organs during a surgical pneumothorax was not well understood. Thus shock and cardiac failure were common causes of death attending operations on the thoracic esophagus. Infections of the mediastinum and pleural cavity persistent pneumothorax, pneumonia and hemorrhage were other causes contributing to the

<sup>1</sup>Heflicien's patient committed suicide; Torek's patient lived 3 1/2 years and died of pneumonia.

<sup>2</sup>From the Department of Surgery of the University of Chicago. Presented before the Clinical Congress of the American College of Surgeons, Chicago, October 1-4, 1940.

high mortality of these operations. Thus for obvious reasons treatment of this tumor was relegated to the roentgenologist for several years.

The above described pathological characteristics of this tumor provide ample reason for the poor showing of irradiation therapy. Although some definite effect on the tumor is evident with this type of treatment, destruction of the entire wall of the esophagus by the lesion precludes the establishment of a permanent cure. A report by Watson in 1936 included the results in 666 patients receiving deep x-ray therapy at the Cancer Memorial Hospital in New York City. Of 68 patients receiving the most recent advantages of this therapy, 33 were alive at the time of the report, 8 for 1 year and 2 for 2 years. Of the remainder treated earlier, the average length of life was only 4.8 months.

The recent revival of interest in the surgical treatment of esophageal carcinoma is both timely and deserving. Its importance is more fully appreciated in view of the fact that it is fourth in frequency of all malignant tumors occurring in men over 20 years of age. In a survey compiling 124,827 autopsies from 42 German pathological institutions between 1925 and 1933, Dormann found it was surpassed in frequency only by cancer of the stomach, lung, and rectum. Of 23,139 deaths due to malignancy in patients over 20 years of age, 8 per cent were due to this tumor.

A major contribution in the recent success enjoyed by surgery in the treatment of this tumor has been by animal experimentation carried out in conjunction with clinical experience. Aided by the establishment of

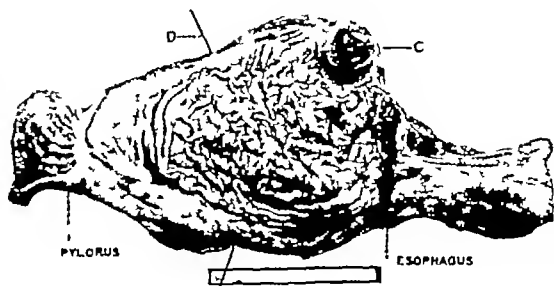


Fig 1 Photograph of autopsy specimen 3 days following resection of lower end of the thoracic esophagus and gastro-esophagostomy for esophageal carcinoma. There was no leak at the site of anastomosis. The patient, a 60 year old man, died of cardiac failure, cerebral damage, and sepsis. The cardiac end of the stomach was closed by pursestring suture at C. The portion of the stomach above D remained in the chest following the resection.

surgical principles especially applicable to this field, and by the improvements of surgical methods, resection of the esophagus in animals was attended by a high degree of success (Miller and Andrus, Saint and Mann, Ohsawa, Adams et al., 2, and Carter et al.). In general the experiments have been divided into two groups, viz (1) resection of the esophagus without re-establishing the continuity of the digestive tract, and (2) resection of a segment of lower esophagus with or without a portion of the cardia and reuniting the esophagus and stomach by suture. Various approaches were tried, one through the lower left thoracic wall receiving the most favor. Again, various techniques were used for making the anastomosis.

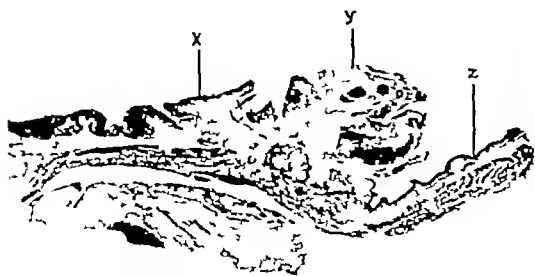


Fig 2 a, left, and b. Microscopic appearance at site of anastomosis seen in Figure 1. Considerable healing has



already resulted. X, the wall of the stomach, Y, the anastomosis, Z, the esophagus.

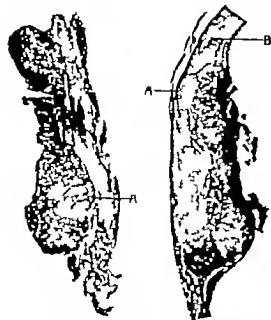


Fig. 3. a, left, and b, microscopic sections of squamous cell carcinomas of esophagus. Note invasion of entire all of the organ by the tumor at A, thus if destroyed by irradiation no lumen could remain. Resection in each case as followed by an unsuccessful anastomosis. Note marked hypertrophy of muscle of esophagus above tumor at B in Fig. 3, b resulting from obstruction of the passage by the tumor.  $\times 3$ .

In performing these experiments, a number of important factors were recognized:

1. An interrupted two-row suture technique gave the most satisfactory results. Some degree of stenosis at the point of anastomosis resulted when a continuous suture was used. Thus the anastomosis was made similar to that of an end-to-side enter-enterostomy with the exception that interrupted sutures are used instead of a continuous suture.

2. Tension on the suture line of the anastomosis was one of the major causes of its failure to remain intact. This could be obviated by drawing enough stomach into the thorax to obtain complete relaxation at the point of the anastomosis. Stay sutures on either side of the anastomosis may also be of value in relieving tension. When any considerable degree of tension was present, leakage from necrosis at the line of suture could be expected.

3. Postoperative mediastinitis and pleuritis due to contamination at the time of operation was minimized by careful walling-off about the field of operation. An end-to-side type of anastomosis rather than an end-to-end union decreased the likelihood of contamination. For this reason the lower end of the esophagus or the cardiac end of the stomach was closed and the fundus of the stomach used for anastomosis with the upper end of the esophagus.

4. Trauma to the vagi should be avoided during the mobilization of the esophagus. Much more postoperative vomiting was observed when the vagi were unduly traumatized or divided during the resection.

5. Mobilization should include only that part of the esophagus to be resected thus interfering with as little as possible of the blood supply to the cut end of the esophagus to be used for the anastomosis. Aseptic necrosis with resultant leak at the site of the anastomosis was much less likely to occur when this was observed.

#### CLINICAL APPLICATION

*Pre-operative preparation of the patient.* This is an important factor and has contributed much to the success of the operation. Since many of these patients are both dehydrated and undernourished when first observed, normal saline solution alternating with 5 per cent dextrose solution administered intravenously is advisable for a few days preceding operation. In cases in which obstruction is less severe a high caloric liquid diet will improve the patient's general condition. The blood count is usually lowered and a transfusion is advisable. In some cases a preliminary jejunostomy may be desirable.

*Anesthesia.* The choice of anesthesia is very important (8-10). Great stress has been placed by some authors on the necessity of intratracheal positive pressure anesthesia for intrathoracic operations. The importance of this type of anesthesia in some instances is not to be denied. It has also undoubtedly given surgeons a sense of security in the carrying out of intrathoracic operations. It has long since been known, however that most intrathoracic operations may be performed

and some with greater ease, under simple mask gas-oxygen (particularly ethylene or cyclopropane-oxygen) inhalation anesthesia under slight positive pressure, the pressure obtained thereby being ample for maintaining inflation of the lungs for the necessary gas exchange. It also allows for sufficient relaxation of the lung to give adequate exposure for carrying out the operative procedures, a factor which cannot be overemphasized. The danger of introducing mouth organisms into the tracheo-bronchial tree during intrabronchial intubation with resultant postoperative pneumonia has been discussed by some (Rienhoff) authors and it is a factor to be kept in mind. Ohsawa has emphasized the value of free open thoracotomy for operations on the thoracic esophagus because of better exposure with relaxation of the lung. We have used simple mask ethylene-oxygen anesthesia for various intrathoracic operations and have found it to be entirely satisfactory. When the operation is completed the remaining surgical pneumothorax is obliterated by aspiration of the air through a catheter drain rather than by distention of the lung with a high positive pressure.

*Prevention of infection.* Since infection is one of the major hazards of this operation every precaution should be taken not only to prevent contamination of the pleural cavity or mediastinum but of the chest wall as well. Complete walling-off with warm moist sponge pads will prevent gross contamination during the resection and resuture when an anastomosis is made. The contents of the esophagus are prevented from spilling into the field either by the use of a small sponge inserted into its lumen, by a fairly loose tie of tape just above the upper cut end of the esophagus, or by the application of a very soft clamp. The latter two are more satisfactory since they prevent constant oozing of blood which tends to obscure the field. Soiling is less apt to occur when an end-to-side anastomosis between the esophagus and the fundus of the stomach is used. In this respect attention must be called to the blood supply of the esophagus and the stomach. Necrosis of the fundus of the stomach following ligation of the coronary smister artery of the lesser curvature

TABLE I — SUCCESSFUL RESECTION OF ESOPHAGUS FOR CARCINOMA

Period	Cases	Remarks
Before 1934	14	All patients except Torek's died within 2 years after operation. His patient lived 13 years dying of pneumonia.
1934-1938	15	
1938-	34	20 living some up to 4 years = 58+ per cent. About 50 per cent of 68 operations were successful.

Relative recent advancement in the surgical management of this tumor

has been reported by Kirschner and others. Ohsawa has also emphasized this danger. However, the results of our experiments and experiences of American surgeons have not substantiated these earlier observations.

When no anastomosis is made, protection of the upper cut end of the esophagus by a rubber cot will help to minimize contamination of the mediastinum when the upper segment is drawn up through a low cervical incision.

*Operation.* To von Mikulicz, Sauerbruch, Zaaiger, Torek, and Lilienthal (13, 14) much credit is due for the development of the operative treatment of carcinoma of the esophagus. Although a large variety of operations have been devised, only two have been extensively employed with success. For tumors located in the middle and upper portions of the esophagus, the operation developed and used by Torek in the first successful resection in 1913 has remained the procedure of choice. This entails the division of the esophagus below the site of the tumor, inversion of the lower end by pursestring sutures and drawing the upper end with the tumor out through a low cervical incision. This is connected with a gastrostomy tube sometime later, thus enabling the patient to eat and to swallow his food through the artificial esophagus.

The second type of operation is employed when the tumor is located in the lower portion of the organ. Following the resection of that portion of esophagus involved by the tumor along with a portion of the cardia in some cases, the fundus of the stomach is brought into the thorax through an opening in the diaphragm and united with the esophagus by suture. Thus the continuity of the digestive tract is re-

TABLE II—COMPARISON OF RESULTS OF TWO TYPES OF OPERATIONS (1918-1940)

Surgeon or clinic	Operation*		Successful cases		Length of survival	Cause of death	Now living (patients)
	A 5 mm.	B 5 mm.	A 5 mm.	B 5 mm.			
Alexander							A, 11 mm.
Bird					4-6 mm.	Diabetic cases (most serious)	
Carter					A-4 mm. B-6 mm.	Stricture Metastasis (large mass)	A 16 mm. B 20 mm.
Chenckoff							A B
Eggers				(reported)	B-7 mm. B-7 1/2 mm. B-8 mm.	Metastases Metastases Metastases	B 8 mm.
Garlock		10			B-8 mm. B-11 mm. B-11 1/2 mm. B-15 mm.	Recurrence Recurrence Metastases Metastases Metastases Metastases	A 77 mm. B 17 mm. B 7 mm. B 7 mm.
Marrash							A 8+ mm.
Ochsner							+ 10
Owen					A-4 yr.	Metastases	A 20 mm.
Scott							B + yrs
University of California				(reported)	A-4 mm. B-4 mm.	Metastases Cystic metastasis	A 10 mm. B 10 mm.
University of Chicago					B-4 yr.	Metastases or recurrence	A 10 mm. B 10 mm.
Total	67		14 + 17 = 31				+ 10 + 17 = 27

\* 5 mm. = with transsection. 1 mm. = without transsection.  
Although the Totals appearing double the number of the operations, the number living at present was about equal. The mortality was approximately the same for each — 50 per cent.

established. The approach for the second type of operation is made through the lower chest wall (seventh rib bed) on the left side. This site may also be used for the first type and has the advantages over the right side approach in that either operation may be decided on after the lesion is exposed and also that glands at the lesser curvature may be resected through an opening in the diaphragm.

**Postoperative management.** This should include maintenance of adequate water and mineral balance and for the first week following operation fluids should be administered intravenously and subcutaneously. A blood transfusion as a routine both during and immediately following operation will help to prevent shock and will hasten convalescence. Oxygen therapy is indicated in the presence of cardiac embarrassment. In those cases in which there is re-establishment of the continuity of the digestive tract, nothing by

mouth is advisable for at least 4 to 5 days during which time fluids and nourishment are given through a jejunostomy tube or by intravenous administration. (Garlock has dispensed with gastrostomy or jejunostomy successfully.) Continuous siphon drainage applied to a stab wound drain of the pleural cavity will not only prevent an accumulation of exudate but will maintain the lungs in complete expansion, both of which are requisites for rapid healing and a smooth postoperative course. The siphonage need not be more than 25 to 30 centimeters of water and may be easily obtained by the use of a double Wangenstein apparatus.

The recent advance in the surgical treatment of this tumor brought about by investigative studies and advanced clinical methods is strikingly demonstrated in the following statistics. Whereas only 14 successful resections were reported up to 1934, during

the next 4 years 15 cases were recorded and 34 more have been collected from reports and personal communications since 1938. This latter number is far from complete since correspondence was carried out with only 40 American surgeons and with no surgeons from foreign countries. The 34 successful resections were made from 68 operations by 12 surgeons, thus an operative mortality of 50 per cent. Of the 34 cases 20 or 58+ per cent are now living as long as 4 years following operation.

It is interesting to note that resection of an esophageal carcinoma accompanied by gastro-esophagostomy carries no more risk than resection of the thoracic esophagus alone. Since approximately 45 per cent of the tumors are located in the lower one-third of the esophagus, re-establishment of the continuity of the digestive tract is possible in a large percentage of cases without additional risk.

This report is being made without undue optimism. Although definite progress has been effected much remains to be desired. For a tumor ranking so high in incidence, many more operable cases should be receiving proper therapy. According to Watson 300 people die of cancer of the esophagus each year (3.5 per cent of all cancer deaths) in New York City. Other cities report even higher percentages. The United States vital statistics for 1938 record 4,871 deaths in Chicago due to cancer and other malignant tumors. About 5 per cent or 245 deaths would represent those due to esophageal carcinoma.

Diagnosis is usually not difficult when once the tumor is suspected. Dysphagia in patients over 35 years of age is due to cancer of the esophagus in a high percentage of cases and must be treated as such until proved otherwise. Fluoroscopic and roentgenological examination following the ingestion of barium will demonstrate evidence of obstruction in the presence of tumor. Esophagoscopy and

biopsy of the obstructed region will lead to a correct diagnosis. Before real progress in the cure of this lesion can be effected it is essential that the profession as well as the laity be educated as to the high incidence of the lesion, the need for early diagnosis, and the fact that successful surgical treatment is possible.

#### BIBLIOGRAPHY

- 1 ADAMS, W. E. The pathological consideration relating to the early diagnosis and curative surgical treatment of carcinoma of the esophagus. *Internat Abstr Surg* (In press).
- 2 ADAMS, W. E., ESCUDERO, L., ARONSOHN, H. G., and SHAW, M. M. Resection of the thoracic esophagus. *J Thoracic Surg*, 1938, 7, 605.
- 3 ADAMS, W. E., and PHEMISTER, D. B. Carcinoma of the lower thoracic esophagus. *J Thoracic Surg*, 1938, 7, 621.
- 4 CARTER, N. B., STEVENSON, JEAN, and ABBOTT, O. A. Esophagogastrostomy. *J Thoracic Surg* (In press).
- 5 DORMANN, E. Das Oesophagus carcinom. *Zeitschr f Krebsforsch*, 1939, 49, 86.
- 6 GARLOCK, J. H. Surgical treatment of carcinoma of thoracic esophagus. *Surg, Gynec & Obst.*, 1940, 70, 556.
- 7 MILLER, R. T., JR. and ANDRUS, W. D. W. Experimental surgery of thoracic esophagus. *Bull. Johns Hopkins Hosp*, 1923, 34, 109.
- 8 OCHSNER, ALTON, DE BAKEY, MICHAEL, and MURRAY, SAMUEL. Surgical aspect of carcinoma of the esophagus. *J Thoracic Surg* (In press).
- 9 OHSAWA, T. The surgery of the esophagus. From the surgical clinics of Prof. R. Torikata and Prof. Isobe, Kyoto Imperial University, 1934.
- 10 PHILLIPS, F. J., LIVINGSTONE, H. M., and ADAMS, W. E. A clinical consideration of anesthesia in intra-thoracic operations. *Anes & Anal* (In press).
- 11 RIENHOFF, F. R. Graded pneumonectomy in the treatment of tumors of the lung. *Bull. Johns Hopkins Hosp*, 1939, 64, 167.
- 12 SAINT, J. H., and MANN, F. C. Experimental surgery of the esophagus. *Arch Surg*, 1929, 18, 2324.
- 13 SAUERBRUCH, F., and O'SHAUGHNESSY, L. Thoracic Surgery. P. 336. Baltimore: Wilham Wood & Co., 1938.
- 14 SAUERBRUCH, F. Die Chirurgie des Brustteils der Speiserohre. *Beitr z klin Chir*, 1905, 46, 405.
- 15 TOREK, F. The first successful case of resection of the thoracic esophagus. *Surg, Gynec & Obst*, 1913, 16, 614.
- 16 Idem. *Arch Surg*, 1925, 10, 328.
- 17 WATSON, W. L. Carcinoma of the esophagus. *Surg, Gynec & Obst*, 1933, 56, 884.

## TREATMENT OF TRAUMAS OF SKIN AND SUBCUTANEOUS TISSUES

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IT has been said that beauty is only skin deep. This statement may be true in individuals who have not suffered trauma but when trauma has occurred beauty or loss of beauty of the skin depends largely on the repair of the subcutaneous soft parts and occasionally of the underlying osseous structures. The loss of beauty in old age is in part due to the atrophy of the fat and connective tissues.

I have become convinced that many of our failures in the treatment of acute traumas of the skin and soft parts are due to lack of appreciation of the pathology occurring in the subcutaneous fat and connective tissues. I desire, therefore, to present certain types of failures and to suggest methods of treatment that will improve the end results. To facilitate the discussion the following types of traumas will be presented: (1) severe contusions of the skin and soft parts; (2) lacerated wounds of the skin presenting a consideration of primary and delayed primary closure; (3) avulsion wounds of the skin and subcutaneous tissue; (4) lacerated tendons, presenting the criteria for immediate and late suture.

The following examples are illustrative of the types of failure due to the initial treatment in injuries of the skin and subcutaneous tissues. It is relative to these failures that I desire to present some of the later advances in surgical therapy.

We have all treated lacerated wounds after what seemed to us satisfactory débridement and suture and have been alarmed at the onset of rapid infection with loss of tissue beneath, the delay in healing or occasionally a more tragic end.

Another type of case which we have all seen, for example is illustrated by a patient admitted to the City Hospital of New York with an avulsion injury of the thigh immediately

above the knee. The skin and soft tissues had been rolled downward as a stocking. Despite careful cleansing, débridement and loose suture infection and gangrene of the skin resulted.

All of us have seen avulsion injuries of the dorsum of the hand and foot, in which gangrene of the skin has resulted despite careful toilet and suture.

Tendons united with extreme care often apparently heal and the patient is discharged from the hospital, but we learn on follow-up that in the meantime the wounds have opened and that pieces of necrotic tendon have been extruded.

As the common failures have been listed, it is in order to approach each type of injury from our knowledge of the pathology involved and to present improved methods of therapy.

### CONTUSED WOUNDS

The success or failure of the general treatment of contused wounds of the skin depends largely on tissue tension. If an artery even of relatively small size, is ruptured during the injury the extravasation of blood into the tissues increases the tissue tension, producing thrombosis of the veins, thus leaving the tissues susceptible to infection.

Severe contused wounds which produce hemorrhage beneath the surface should be carefully watched. In severe contusions, Babcock advises releasing incisions down through fascia on each side of the injury in order to relieve tension and allow the extravasation of the collected serum. In cases in which the trauma is not as severe as he has described, the aspiration of the hematoma beneath the skin may be sufficient. Such wounds demand surgical judgment and excellent operative technique. If one hesitates when necrosis is beginning, one may lose large areas of tissue. If the patient is seen early and is in a satisfactory condition, small and deeply contused

wounds may be treated by excision of the traumatized area and primary suture

#### LACERATED WOUNDS

The treatment of lacerated wounds of the skin and subcutaneous tissues is dependent on first, the age and general condition of the patient, second, the condition of the skin at the time of injury, third, the type and cleanliness of the instrument producing the injury, and, fourth, the length of time elapsing from injury to operation. While these conditions are elementary and generally known, they are not always given the attention they deserve.

1 *The age and condition of the patient* It is advisable in obtaining the history to get the patient's reaction to previous traumas. There are some patients who, despite severe injuries in the past, have been resistant to infection, and it is logical to assume that they may be resistant in the present emergency. Others have shown susceptibility to infection and must be treated in a much more conservative manner.

2 *The condition of the skin* Whether the skin is clean or dirty at the time of injury and also the location of the injury are important factors in our consideration of treatment of soft parts. Braine, in his discussion of primary suture, states that buttock wounds and wounds of the leg should not be treated by primary suture, as they are more susceptible to infection, due to location and blood supply. The wounds over the tibia are obviously slow of healing and need careful watching.

3 *The instrument* The type of instrument producing the injury is important, as a sharp instrument causes less surrounding tissue trauma than a blunt one, which creates necrosis and hemorrhage of the deeper connective tissue structures, as well as lacerations of the skin.

4 *The lapse of time* The length of time elapsing from injury to operation is of significance. Bruning quotes the well known experiment of Friedrich showing that there is a lag period in bacterial growth for about 6 hours. During this period the wound may be excised with little fear of bacterial spread. After this time the bacterial growth is so increased that

it is difficult to obtain by débridement a relatively clean field.

The present trend in surgery in preparing a contused or lacerated wound for treatment is to avoid, in so far as possible, the active antiseptic, as it is felt that an antiseptic strong enough to kill bacteria is also apt to destroy the resistance of the living cells of the host. Many writers advise the careful washing of the wound, followed by the use of antiseptics on the neighboring skin. There are others, however, who believe that simple washing, with white soap and water for many minutes is sufficient. The author favors the method of copious gentle washing of the wound with soap and water. The wound is then protected by gauze dressing, after which the skin is prepared by cleansing with soap, water, ether, and alcohol, and the wound is again lavaged.

The foreign literature, and particularly the French literature, of the present war concerns itself especially with a discussion of primary versus delayed primary suture in lacerated wounds. While this problem has not arisen so much in civil surgery, nevertheless it is of vital import and it might be well to review some of the opinions that are expressed today. Braine, in an article on primary suture of war wounds, summarizes the situation as follows. He states that "primary closure is contraindicated when the circumstances are not ideal, when the wound is not recent, when the surgical equipment is imperfect, when the operator is not experienced, and when the injured cannot be closely followed for at least 2 weeks." He presents the following general instructions:

"All primary sutures entail a certain risk and should never be lightly performed. They should not be done as a routine measure—each case should be considered on its merits. Suture should not be performed unless all conditions are favorable as regards the wounds, patient, surgeon's experience, and the military situation. Primary suture following excision is always a delicate operation upon which the patient's life may depend. Suture is not indispensable to save the patient's life, on the contrary, it may result in fatal accidents. Every unsuccessful suture aggravates the original condition. Meticulous excision of the wounded area, and not the suture itself, is the essential feature. The suture may be performed later at leisure with a greater margin of



## TREATMENT OF TRAUMAS OF SKIN AND SUBCUTANEOUS TISSUES

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IT has been said that beauty is only skin deep. This statement may be true in individuals who have not suffered trauma, but when trauma has occurred beauty or loss of beauty of the skin depends largely on the repair of the subcutaneous soft parts and occasionally of the underlying osseous structures. The loss of beauty in old age is in part due to the atrophy of the fat and connective tissues.

I have become convinced that many of our failures in the treatment of acute traumas of the skin and soft parts are due to lack of appreciation of the pathology occurring in the subcutaneous fat and connective tissues. I desire therefore to present certain types of failures and to suggest methods of treatment that will improve the end results. To facilitate the discussion the following types of traumas will be presented: (1) severe contusions of the skin and soft parts; (2) lacerated wounds of the skin, presenting a consideration of primary and delayed primary closure; (3) avulsion wounds of the skin and subcutaneous tissue; (4) lacerated tendons presenting the criteria for immediate and late suture.

The following examples are illustrative of the types of failure due to the initial treatment in injuries of the skin and subcutaneous tissues. It is relative to these failures that I desire to present some of the later advances in surgical therapy.

We have all treated lacerated wounds after what seemed to us satisfactory débridement and suture and have been alarmed at the onset of rapid infection with loss of tissue beneath, the delay in healing or occasionally a more tragic end.

Another type of case which we have all seen, for example is illustrated by a patient admitted to the City Hospital of New York with an avulsion injury of the thigh immediately

above the knee. The skin and soft tissues had been rolled downward as a stocking. Despite careful cleansing, débridement, and loose suture infection and gangrene of the skin resulted.

All of us have seen avulsion injuries of the dorsum of the hand and foot, in which gangrene of the skin has resulted despite careful toilet and suture.

Tendons united with extreme care often apparently heal and the patient is discharged from the hospital, but we learn on follow-up that in the meantime the wounds have opened and that pieces of necrotic tendon have been extruded.

As the common failures have been listed it is in order to approach each type of injury from our knowledge of the pathology involved and to present improved methods of therapy.

### CONTUSED WOUNDS

The success or failure of the general treatment of contused wounds of the skin depends largely on tissue tension. If an artery even of relatively small size is ruptured during the injury the extravasation of blood into the tissues increases the tissue tension, producing thrombosis of the veins thus leaving the tissues susceptible to infection.

Severe contused wounds which produce hemorrhage beneath the surface should be carefully watched. In severe contusions, Babcock advises releasing incisions down through fascia on each side of the injury in order to relieve tension and allow the extravasation of the collected serum. In cases in which the trauma is not as severe as he has described, the aspiration of the hematoma beneath the skin may be sufficient. Such wounds demand surgical judgment and excellent operative technique. If one hesitates when necrosis is beginning one may lose large areas of tissue. If the patient is seen early and is in a satisfactory condition, small and deeply contused

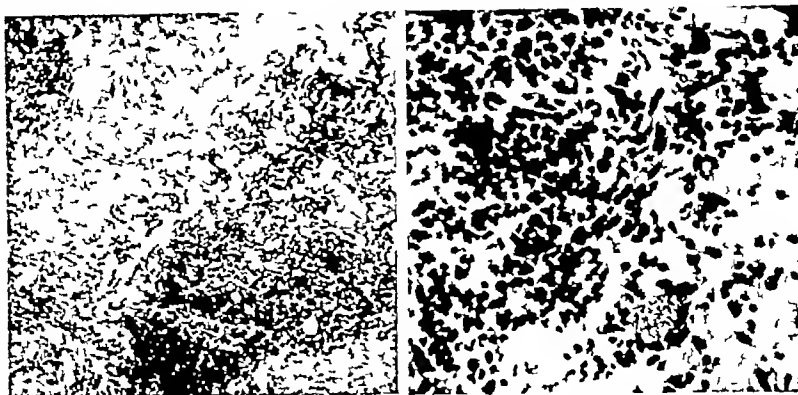


Fig 5, left Photomicrograph of biopsy specimen taken from wound surface 48 hours after operation at time of delayed closure (Courtesy of Coller and Valk, *Ann Surg*, 1940, 112 260)

Fig 6 Same as Figure 5

"Fraser, in 1918, reported an incidence of 9.7 per cent failure in 41 cases of primary closure as compared with 4.5 per cent failure in 63 cases of delayed primary suture. He also reported 31 bacteriologically negative wounds from 35 contaminated wounds after 48 hours' treatment by delayed primary closure employing a flavine pack in the wound. In 1918 delayed primary closure of all soft-tissue wounds, excepting those in the scalp, face, and hands, was advised by the surgeons of the American Expeditionary Force. The best results were obtained when the wounds were closed within 50 hours."

Coller's method is to suture loosely the muscles and fascia beneath the fat and the skin. After careful cleansing and débridement of the fat and subcutaneous tissues, fine silk sutures are inserted in the skin but left untied, and the wound is packed from each end with acriflavine gauze down to the fascia. In 24 to 48 hours the pack is removed and the sutures are tied. He presents a series of 21 cases treated in this manner, with only 1 minor infection. I have had the opportunity of using this method 8 times successfully. Coller presents microscopic sections of the wound edges in 24 hours and states that the sections show a residue which consists of fibrin, in the meshes of which are polymorphonuclear leucocytes, wandering cells, some necrotic tissue, and many fibroblasts (Figs 1-6). As cultures taken from the wound at the time of operation and at the time of closure do not show destruction of the bacteria by this method, it must mean that two important surgical principles are involved: (1) the release of tension in the wound by leaving it

wide open, and (2) the stimulation of the reparative process of the wound or the creation of bacteriostasis by the presence of gauze soaked in acriflavine. He believes that after the coagulation of the fibrin the resistance of the wound is greatly increased because of the sealing off of the capillary and lymph spaces, which tends to keep infection localized or below the clinical horizon.

In discussing the paper of Coller, McClure suggested that part of the success of this method might be due to the inhibitory effect of the air upon the growth of anaerobic organisms, as well as its bacteriostatic effect on the aerobic bacteria.

One might summarize the problem of primary or secondary closure of lacerated wounds as follows. Primary closure may be attempted if the patient is healthy, the skin clean, the instrument creating the damage relatively clean and sharp, and if the patient is seen well under 6 hours after the injury. The surgeon performing the operation must use meticulous care in lavaging the wound and in gentle excision of all traumatized areas. Sutures must be inserted in order to avoid dead spaces, but with care that there shall not be tension when the secondary edema occurs following the operative procedure. Plaster encasement or adequate splinting should be utilized to prevent muscle pull and production of hematomas. Delayed primary suture should be performed in the event that the aforementioned criteria are not present.



Fig. 1, left. Acriflavine pack being placed in wound. (Courtesy of Collier and Valk, *Am. Surg.*, 940, 260.)

Fig. 2. Acriflavine pack in place. (Courtesy of Collier and Valk, *Am. Surg.*, 940, 260.)

safety. Excision followed by suture is a procedure of patience, care, and thoroughness. The wound should be scrupulously examined before the tissues are approximated. In doubtful cases it is better to apply dressings and drains. Primary sutures require careful watching up to complete clottrization, and the surgeon must be prepared at any moment to remove the sutures. The small extent of the surface of injury may not be an indication of the amount of deeper injury which would always be determined. Primary suture without drainage is exceptional in wounds of the buttocks, thigh, and calf. Primary delayed or secondary suture is worthy of increased attention although the results are less brilliant the method is safer.

Bruning states that the most important feature in after treatment is immobilization, which should be carried out as in the case of a fracture in order to prevent any displace-

ment of the tissues in relationship to one another.

Gregoire, Chevassu, Lenormant, Gosset, and Roux Berger all warn of the dangers of primary suture in war wounds. While they admit that the few spectacular cases make one attempt to utilize the procedure the failures more than militate against these successes.

In this country Collier has recently presented a very interesting series of cases of potentially contaminated wounds which he has treated by delayed primary suture. His discussion is largely one relative to the possible infection of abdominal wounds from contamination beneath the surface, but the surgical principles are the same as one finds in lacerated wounds. Collier says



Fig. 3, left. Photomicrograph of biopsy specimen taken from wound 24 hours after operation at time of delayed closure. (Courtesy of Collier and Valk, *Am. Surg.*, 940, 260.)

Fig. 4. Same as Figure 3.

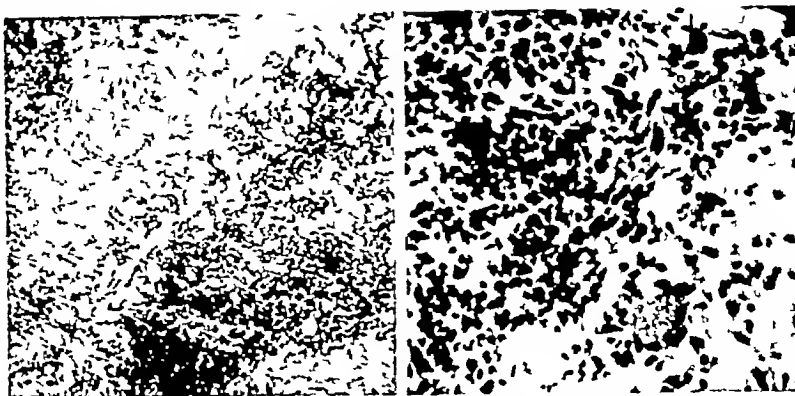


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Fig. 7. Immediate postoperative appearance. The immobilized, immobilized plaster encasement as necessary because of fracture (Courtesy of Farmer *J. Surg.* 930, 95.)

It is obvious that there is a third type of injury which I have not mentioned because it seems evident to me that one would not attempt either primary or delayed primary suture that is, the type of injury in which there is extensive tissue damage and in which it is evident that the wound must be debrided and left wide open for healing by granulation. In this type, immobilization of the neighboring joints is often a necessity in order to prevent constant trauma by muscular action. Because of its severity the lesion may need various therapeutic measures. Dakinization or vaseline gauze packing as by the Orr method, may be the therapy of choice. Early skin grafting is advisable as soon as the granulations permit.

#### AVULSED WOUNDS OF THE EXTREMITIES

Farmer has postulated what seems to the author to be an adequate theory of the cause of failure in avulsed wounds. He states that when the skin and subcutaneous fat are avulsed thrombosis of the venous and lymphatic vessels is produced by the trauma. On the other hand the arterial vessels are not as easily injured, and they continue to pump blood into the traumatized zone. When the

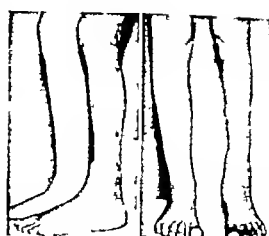


Fig. 8. Front and side view of final result (Courtesy of Farmer *J. Surg.* 930, 95.)

pressure of the incoming blood overcomes the normal tissue pressure necrosis occurs as the smaller arteries begin to thrombose. We are accustomed to see a similar pathological process in the pre-gangrenous stage of acute cholecystitis. All surgeons are conversant with the appearance of the bluish gall bladder which is swollen and edematous and which one is apt to call beginning gangrene. Sections of such gall bladders, however, show the tissue full of extravasated blood. The initial process has probably been a venous occlusion due to pressure of an impacted stone in the cystic duct. As the tissue pressure increases, the artery gradually becomes thrombosed and then, and not until then, does active gangrene occur. Fortunately for the gall bladder omental adhesions are apt to bring relief from some of the tissue tension.

If Farmer's theory is true his method of treatment is a real advance in the handling of avulsed wounds. He believes in the excision of all of the avulsed skin, for he says that if a portion of the skin is left attached the arteries will continue to pump blood into the skin and subcutaneous tissue and gangrene will result. When the skin has been removed the assistant carefully debrides the underlying structures, removing all dead or traumatized tissue. Farmer advises the cleaning of the raw area with aseptic rather than antiseptic fluids. Thus soap and water and saline are the solutions of common choice. The surgeon removes



Fig 9 The result 2 weeks after accident (Courtesy of Farmer, *Ann Surg*, 1939, 110 952)

the avulsed skin. It is held on a firm flat surface and the fat is removed by scraping or by cutting with curved scissors well into the dermis. After the combined procedure of débridement of the deeper structures with complete hemostasis and excision of the subcutaneous fat, the skin is then sutured accurately into the defect from which it was removed. To prevent dead spaces, quilting sutures are used in addition to the circumferential sutures, and the graft is perforated with numerous small stab wounds. The primary dressing is of normal saline. Firm pressure is obtained by bandaging, and a plaster encasement insures immobility. The dressing is changed in 10 to 14 days unless there is a special indication for an earlier examination (Figs 7-10). It was the author's privilege to see a number of cases reported by Farmer, and the results were far superior to anything he had seen in similar wounds treated by other methods.

There may be one refinement which could be added to Dr Farmer's method. J Staige Davis has shown that skin may be preserved for a reasonable period of time by refrigeration. Also, it has been stated that during refrigeration the differences between the portions of the skin that would normally



Fig. 10 The condition some months after accident (Courtesy of Farmer, *Ann Surg*, 1939, 110 952)

live and the portions that are too severely injured to survive are demonstrated. Davis says

"The idea is prevalent that skin grafts of all kinds must be applied either immediately or within a comparatively short time after cutting. Years ago the writer [Davis] became interested in the preservation of skin grafts, and has experimented with the refrigeration of various types. He soon became convinced that there was no hurry in applying skin grafts and that they could be preserved quite simply. If the grafts were to be used within 24 hours, wrapping them in sterilized dressings moistened with normal salt solution to keep them from drying and storing in the ice box were sufficient. If longer periods were required the grafts were stored in jars of sterile oil, vaseline or sterile albolene in the coil compartment of a mechanical refrigerator. The grafts when removed from vaseline or albolene are as pink as when they were put in, and look quite fresh. They are either wiped gently with sterile gauze to remove the vaseline or are washed with ether before being placed on the granulations. It was noted that while the refrigerated grafts would take and the blood supply become established it was fully a week, and sometimes longer, before any new growth of epithelium is observed from the skin margins and that this growth seemed slower than from immediate grafts of similar type. Microscopically no definite change was observed in the graft refrigerated, as above described, even after several months. Immediate autografts are always to be preferred, but refrigerated autografts have a distinct field of usefulness, and excess material can be preserved in suitable cases and used as required. Refrigerated small deep grafts are permanently successful and have been successfully transplanted after several weeks."

The usefulness of Davis' method in avulsion injuries can readily be seen, because there are



FIG. 7. Immediate postoperative appearance. The femoralized, immobilized plaster encasement as necessary because of fracture. (Courtesy of Farmer *Am Surg* 93: 951.)



FIG. 8. Front and side views of final result of Farmer *Am Surg* 93: 951.)

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clinical results of local administration of sulfanilamide are as yet too uncertain either to advocate or condemn. When they have been used, it has been noted that there is an increase in the serous exudate, and this might be distinctly inadvisable if skin grafts are contemplated.

### TENDON INJURIES

Tendons, like innocent bystanders, are subject to accidental injuries involving other structures. Extensive wounds of the skin and subcutaneous tissues frequently cause tendon damage as well. This is especially true of areas such as the dorsum of hands and feet, wrists and ankles, where the covering is thin and the bed unyielding. The most dangerous location for tendon injuries is in the flexor creases of the fingers and palm. This area is frequently traumatized by sharp cutting instruments and the tendons severed. If infection is not prevented, the extension of the pus along the tendon sheath will not only create slough of the tendons but may allow the infection to extend along the deeper spaces of the hand with irreparable injury. The possibility of tendon injury, therefore, must be borne in mind when apparently superficial wounds are treated, and repair of tendons, when injured, should be undertaken at the earliest possible moment consistent with good surgery.

The decision between primary and secondary suture of tendons calls for keen surgical judgment. In cases seen within 4 hours of injury primary suture may be done with reasonable expectation of an excellent result. This assurance is lacking, however, when dirt has been ground into the wound or the tendon extensively contused and devitalized. Primary suture is hazardous also if there is a question of contamination with human acclimatized bacteria or if antiseptics have previously been poured into the wound. In all such cases and in injuries more than 4 hours old, attention should be directed solely to cleansing and healing the wound, and the damaged tendon left for secondary suture at a later date.

When primary suture has been injudiciously performed and infection ensues, the patient is

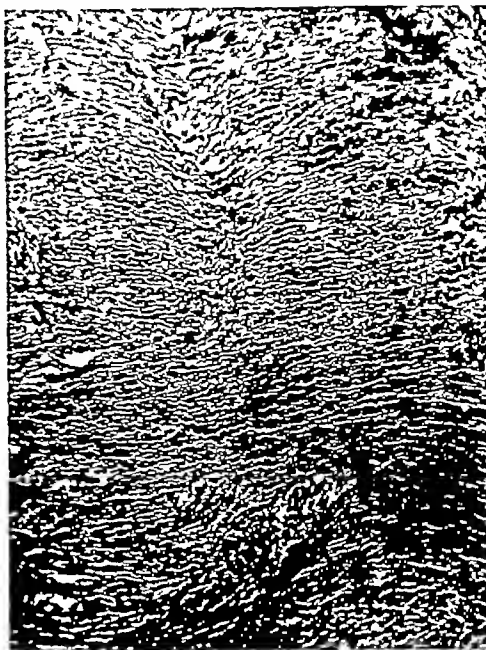


Fig. 13 Dense scar tissue in the region of the deeper area

far worse off from the standpoint of eventual rehabilitation than if the tendon had been left for secondary suture because just so much tendon tissue will have been lost and scar tissue formed. Function is traded for deformity—a poor bargain.

Atraumatic handling of tissues, the avoidance of chemical antiseptics, and the use of fine silk sutures placed without tension are sound surgical principles worthy of particular emphasis in tendon repair. Tendon is a relatively avascular structure, its meager blood supply coming from a delicate sheath or from the surrounding soft tissues. At the time of repair, if the already damaged tissues are needlessly subjected to the additional trauma of rough handling and strong antiseptics or if the blood supply is impoverished by tense sutures, one must not be surprised should infection, with all its disastrous consequences, result.

Kanavel, Bunnell, Koch, Mason, and Loyal Davis have contributed largely to the knowledge of the physiology and histology of tendon repair and have presented for us definite clinical therapeutic measures based on sound





Fig. 1. High power photomicrograph showing edema of the superficial granulating area with slight degree of infection. Numerous blood vessels can be seen.



Fig. 2. High power photomicrograph of section at junction of granulation and scar tissue. Indicates the superficial granulation tissue & the junction of the scar and granulation tissue & the scar tissue.

some cases in which the muscle damage may be so great or the patient seen so late after injury that immediate skin grafting would be inadvisable. However if one can preserve the uninjured skin and transplant it at a later time a great saving can be made in hospital days and in suffering for the patient.

Avulsion injuries of the dorsum of the hand must be treated according to the depth of the injury. When tendons are exposed, immediate covering is essential. The insertion of the hand into an abdominal flap is advantageous when the injury is deep when it is superficial Farmer's method could be carried out by removing the avulsed skin and replacing it as he described. When the skin has been too severely traumatized, a full tissue graft taken from the thigh can be readily used. The replacement of the avulsed skin even if split longitudinally as described many years ago by the Mayo, usually results in failure if any portion is left attached. Full tissue grafts may be readily utilized in similar injuries of the dorsum of the foot, provided the avulsed skin is not satisfactory.

In avulsed wounds that cannot be closed immediately and in which for any reason skin grafting is delayed for over 2 weeks, it is ad-

visable to excise the underlying scar tissue rather than merely to remove the superficial granulations by curette. After several failures from delayed skin grafting following curettage of the superficial granulations, I dissected through the underlying scar tissue which appeared red and healthy on the surface and was surprised to find rubbery firm avascular scar tissue extending often to a depth of 0.4 to 1 centimeter before healthy tissue appeared. Sections taken of this tissue reveal definitely the lack of vascular supply necessary to stimulate epithelization. The grafts appear healthy for a week or 10 days and then gradually melt away (Figs. 11 to 14).

**Chemotherapy.** In discussing the treatment of lacerated and avulsed wounds of the skin and soft tissues it has not seemed necessary to stress the use of sulfanilamide or similar preparations, either by oral or parenteral administration, because these drugs are being used throughout the country at large. Nor does it seem advisable at this time to recommend the local administration of these drugs at the site of injury. The experimental and

clinical results of local administration of sulfanilamide are as yet too uncertain either to advocate or condemn. When they have been used, it has been noted that there is an increase in the serous exudate, and this might be distinctly inadvisable if skin grafts are contemplated.

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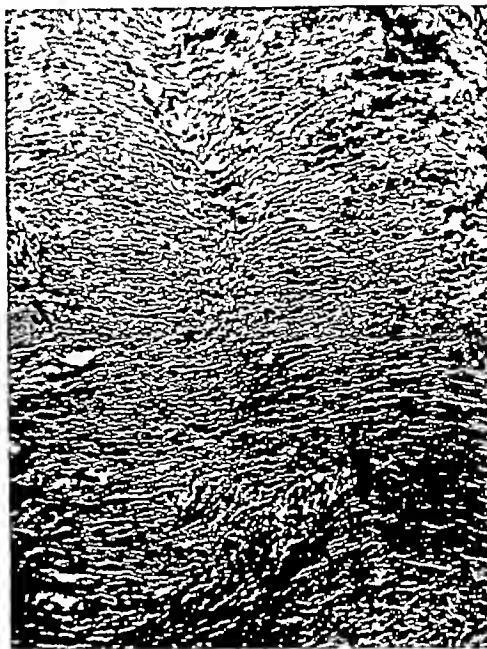


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Kanavel, Bunnell, Koch, Mason, and Loyal Davis have contributed largely to the knowledge of the physiology and histology of tendon repair and have presented for us definite clinical therapeutic measures based on sound

surgical principles. They have shown that connective tissue union takes place first between the apposed ends of a severed tendon. This process commences promptly after suture is complete in 3 or 4 days, and is dependent upon restoration of continuity of the tendon sheath or surrounding soft tissues. In favorable cases tendon cells then grow across this connective tissue bridge and establish a complete tendinous union in from 10 to 14 days. The tendon at first shows distinct thickening at the site of repair and adherence to the surrounding structures but in the course of a few weeks it becomes thinner the adhesions are stretched, and freedom of motion is gradually established to a greater or lesser degree.

Bearing this in mind, one can appreciate the vital importance of an atraumatic technique in tendon repair the use of fine non-absorbable nonirritating sutures placed without tension the elimination of exposed knots, and the accurate reposition of sheaths as well as tendons. Following repair the parts should be splinted in the position of greatest tendon relaxation for a period of 2 to 3 weeks before active or passive motion is attempted. Physiotherapy when initiated must be under the direct supervision of the surgeon who alone, is responsible for the end-result. Too often the importance of this period of rehabilitation is minimized the after care being placed in the hands of enthusiastic but inexperienced assistants. Such a practice cannot be too strongly condemned.

The principles discussed thus far apply to tendon repair in general. Secondary suture calls for special consideration. No attempt at secondary repair of tendons should be made in less than 3 to 4 weeks after injury in a wound which was closed and had healed *per primam*. If a mild wound inflammation or a mild staphylococcal infection was present, 6 to 8 months should be allowed to pass, and in the case of a severe infection or if a streptococcus was cultured it is safer to wait 12 to 18 months before a secondary tendon suture is undertaken. These time limits, are of course not absolute but they serve as a fairly reliable guide to the condition of the tissues and the chances of relighting an infectious process.

Scar tissue in which the tendon ends have become embedded must be carefully but thoroughly removed by sharp dissection. Some times, when subcutaneous tissue is scanty and scar tissue excessive a full thickness or pedicle graft must be transferred to fill the defect left by this dissection in order to have sufficient subcutaneous fat surrounding the tendon to prevent re formation of dense scar tissue adhesions. In this event actual tendon suture must be postponed until a later date.

The tendon ends must be completely freed of adhesions back as far as normal tendon sheath and any portion which cannot be freed will have to be excised. This excision may make it impossible to re-appose the ends of the tendon without tension. If this proves to be the case tendon suture should not be attempted but a free tendon graft, complete with its sheath, must be obtained from an other part of the body and used to fill the gap.

The exercise of sound judgment in the selection of cases for primary suture and courage to delay primary to secondary suture with a clear comprehension of basic surgical principles will, therefore go far toward improving the results of treatment in acute tendon injuries.

#### SUMMARY

1. Hemorrhage and edema can cause extensive tissue necrosis in severely contused wounds. The early releasing of incisions may be necessary.

2. The criteria for and against primary suture in lacerated wounds and the technique to be followed are presented.

3. In order to prevent gangrene of the flap in avulsed wounds, an operation is described by which the skin is debrided and implanted as a full tissue graft in the defect. The possibility of preserving by refrigeration skin that cannot be immediately utilized is discussed.

4. The process of repair of sutured lacerated tendons is presented. The indications for and technique of primary and delayed suture are described.

#### BIBLIOGRAPHY

- BASCOM, W. W. Wounds and their complications. *Am. J. Surg.* 937, 96-97.  
 2. BREWER, C. F. and O'CONNOR, R. J. Jr. The healing of surface wounds for the prevention of deformity. *Ann. Surg.* 923, 98, 394-407.

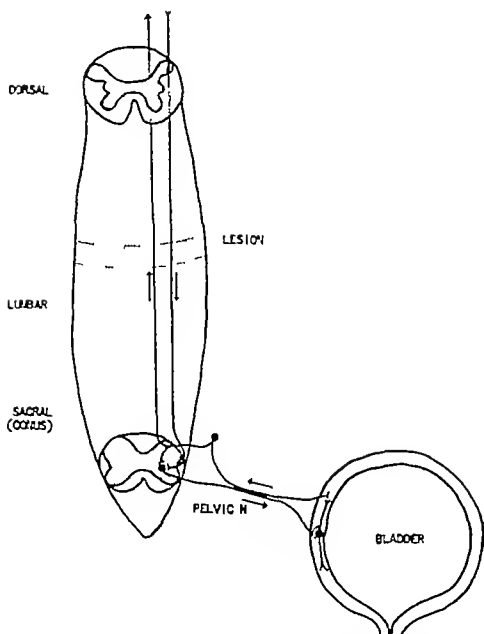


Fig 1 The reflex neurogenic bladder is caused by a complete transecting cord lesion, above the conus. Bladder activity is controlled by a simple spinal reflex, synapsing in the conus. When the bladder fills to a certain capacity (100 to 250 cc), the reflex is stimulated, causing bladder contraction. This bladder is characterized by periodic vacuations, without voluntary control.

Upon the extent and level of spinal injury these are first, the reflex bladder, when the lesion is situated above the conus, leaving the simple spinal reflex arc intact, second, the autonomous bladder, which has been completely denervated by extensive injury of the conus or cauda equina, and, third, the atonic bladder, in which the injury has interrupted only the sensory side of the spinal reflex arc. After complete recovery from the nerve injury takes place, the bladder function ultimately becomes normal, otherwise these patterns are permanent.

The urological management of these cases concerns itself with two different periods: management of the bladder during the period of early atonia, and, second, the management of the chronic neurogenic bladder.

#### THE MANAGEMENT OF THE ACUTE NEUROGENIC BLADDER

Two cardinal dangers in management of the acute atonic neurogenic bladder are in-

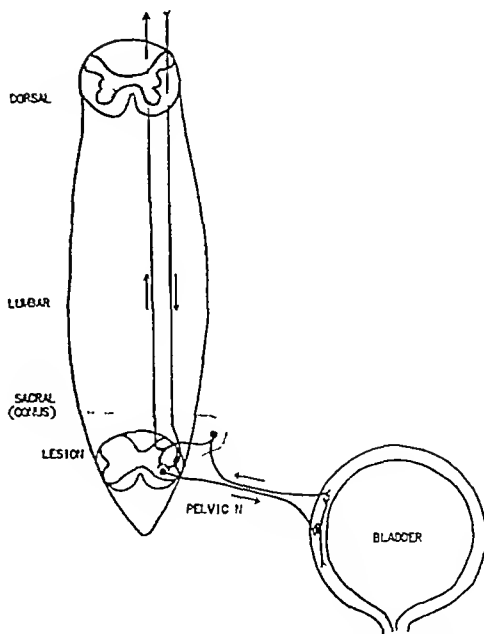


Fig 2 The autonomous neurogenic bladder is caused by any lesion which destroys the conus or cauda equina. The bladder is completely deprived of external innervation, and depends entirely on its intrinsic myenteric plexus, whose fibers lie within the bladder wall. The bladder musculature and internal sphincter both are hypertonic. Despite the high intravesical pressure, the tonic sphincter acts as an obstruction. Since reflex activity is abolished, evacuation occurs only when the intravesical pressure exceeds the sphincteric obstruction. Voiding is by dribbling or overflow. A high residual urine is present.

fection and overflow incontinence. Careful asepsis and proper drainage will minimize both of the dangers. Nursing care of these patients is greatly simplified by drainage of some type, and it has been demonstrated that the incidence of sepsis can be enormously reduced by properly managed drainage. Obviously, the circumstances under which the patient is encountered following injury will be an important factor in deciding the type of drainage employed and when it should be instituted. On the battlefield, the highway, or in the factory, aseptic urinary drainage is usually impossible, in these circumstances, overflow incontinence is more desirable than immediate catheterization. Since the entire management of traumatic myelitis is one which requires the facilities of hospitalization, urinary tract drainage should be deferred until this is accomplished.

# THE MANAGEMENT OF THE URINARY BLADDER IN TRAUMATIC LESIONS OF THE SPINAL CORD AND CAUDA EQUINA

REED M. NESBIT M.D., F.A.C.S. and WILLIAM G. GORDON M.D. Ann Arbor Michigan

**D**ISORDERS of bladder function which always accompany major spinal cord injuries are largely responsible for the high mortality associated with acute traumatic myelitis. This high mortality results from overflow incontinence with the development of decubital ulcers and urinary tract sepsis. Both of these complications can be minimized by proper management.

The rational management of the bladder in these circumstances depends upon a recognition of certain fundamental principles. Spinal shock which follows cord injury is always reflected in the urinary bladder by muscular atony manifested clinically by urinary retention and overflow incontinence. The period of bladder atony is temporary lasting from a few days to many months. Recovery of the bladder is manifested by alterations in its behavior depending upon the extent and location of the cord injury. These alterations in behavior follow certain definite patterns, which may be recognized by appropriate examination.

There are three general types of recovery pattern. The first and most common of these is the reflex neurogenic bladder produced by a transecting lesion above the conus (Fig. 1). In this situation bladder activity is governed by a simple spinal reflex, synapsing in the sacral cord devoid of cerebral control. Filling of the bladder with resultant stretching of its wall constitutes the stimulus which results in bladder contraction and evacuation. This reflex evacuation is necessarily periodic, and since it is anatomically dissociated from the higher centers, is not under voluntary nervous system control. The patient can neither

initiate nor cause cessation of urination at will but is periodically incontinent.

A second pattern of bladder behavior is seen following extensive injury of the conus cauda equina (Fig. 2) with interruption both the sensory and motor units of the reflex arc which controls the bladder. This externally denervated bladder has been properly termed the autonomous neurogenic bladder. Normal sensation is gone and voluntary reflex micturition is abolished. Bladder muscle tone is increased, probably by sympathetic plexus. The internal sphincter is hypertonic. It is possible that this is maintained by the sympathetic via the (presacral) hypogastric nerves which are spared in conus or conus lesions. The bladder always shows coarse trabeculation, an evidence of imbalance between sphincter and detrusor tone and carries a high residual. The intravesical pressure is high, and evacuation is by dribbling overflow since reflex activity is abolished.

The third and last, type of neurogenic bladder results when only the sensory side of the spinal reflex arc is damaged (Fig. 3) which occurs in some partial destructive lesions of the conus or cauda equina. This bladder behaves like the atonic bladder of tabes dorsalis, which by an analogous mechanism the sensory unit of the arc has also been interrupted. Recovery from spinal shock is followed by a persistent atonia of the bladder musculature. There is dribbling overflow incontinence from a bladder which has a low intravesical pressure and which possesses no reflex activity.

To summarize following spinal cord injuries regardless of level, a period of shock with bladder atonia and retention occurs. Subsequently with recovery of neurologic function, one of the behavior patterns of bladder function is manifested depending

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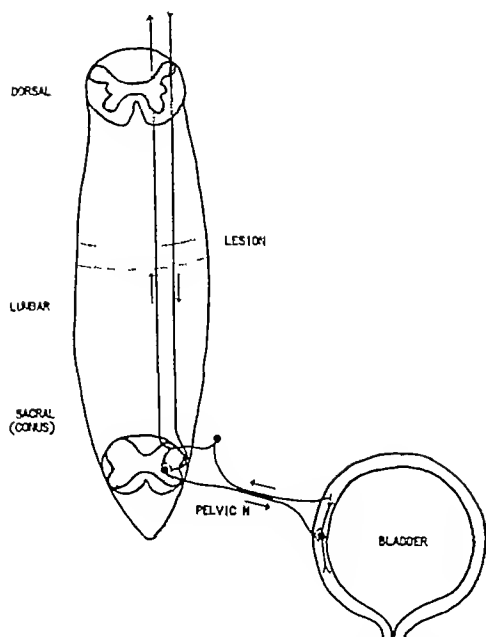


Fig 1 The reflex neurogenic bladder is caused by a complete transecting cord lesion, above the conus. Bladder activity is controlled by a simple spinal reflex, synapsing in the conus. When the bladder fills to a certain capacity (100 to 250 cc), the reflex is stimulated, causing bladder contraction. This bladder is characterized by periodic evacuations, without voluntary control.

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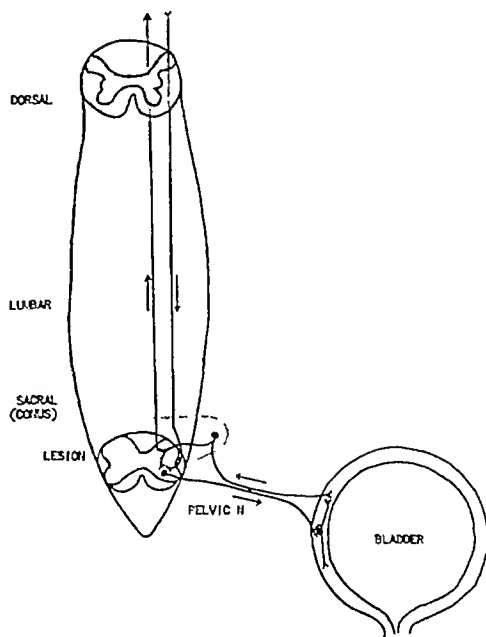


Fig 2 The autonomous neurogenic bladder is caused by any lesion which destroys the conus or cauda equina. The bladder is completely deprived of external innervation, and depends entirely on its intrinsic myenteric plexus, whose fibers lie within the bladder wall. The bladder musculature and internal sphincter both are hypertonic. Despite the high intravesical pressure, the tonic sphincter acts as an obstruction. Since reflex activity is abolished, evacuation occurs only when the intravesical pressure exceeds the sphincteric obstruction. Voiding is by dribbling overflow. A high residual urine is present.

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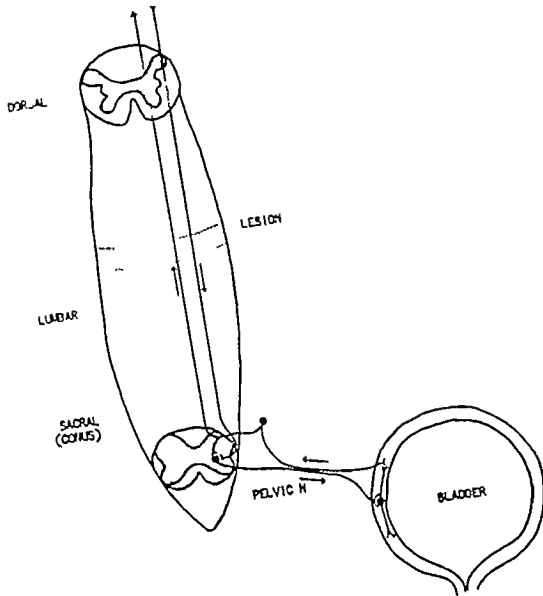


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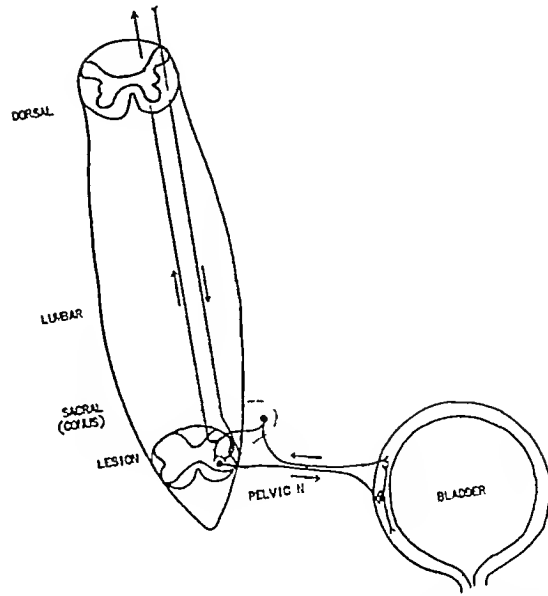


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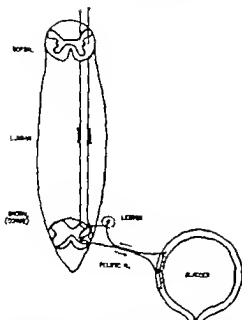


Fig. 3. The toxic neurogenic bladder is caused by a partial injury of cornu or cauda equina in which the sensory pathways alone are damaged. Reflex activity is abolished by destruction of the sensory limb of the spinal reflex. Since sensation is lost the bladder is habitually over-distended until actual atrophy of its musculature results. The expulsive forces then become so weak that normal sphincteric resistance alone causes urinary retention. Voiding is by straining or dribbling overflow with constant high residual urine.

There are three methods of providing bladder drainage: intermittent catheterization, indwelling catheter, and suprapubic cystostomy. Intermittent catheterization is undesirable because it does not provide continuous drainage and frequent catheterization increases the hazard of urethral trauma and fulminating infection. Continuous drainage, either by urethral or suprapubic catheter, provides the optimal condition for avoidance of sepsis and incontinence and for allowing the earliest return of bladder tone. The choice between these two methods of continuous drainage depends upon the hospital facilities available for providing the greatest degree of aseptic care of the drainage systems employed. Under ideal circumstances, urethral catheter drainage might appear preferable in that it avoids the necessity of a suprapubic wound. The inherent dangers of this method are to be found in the occasional severe genital infec-

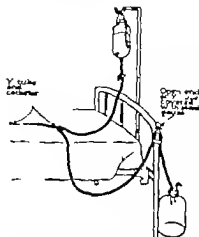


Fig. 4. The closed irrigator-drainage system. The system, wrapped in alcohol, is sterilized by autoclave. reservoir bottle may be filled with any desired antiseptic solution. Periodic bladder irrigations are carried out by closing the upper limb of the Y-tube. When pressure drainage is desired, the upper limb of the Y is kept open and is covered with sterile gauze.

tions which occur with indwelling catheters in the male. It should be borne in mind that the indwelling catheter drains the bladder but not drain the urethra. Suprapubic drainage helps to avoid urethral infection and therefore this method is preferable under most circumstances.

Continuous drainage by either method necessitates the maintenance of an aseptic drainage system if serious urinary infection are to be avoided. This may be provided by a sterile closed irrigator system, such as that employed at the University Hospital (Fig. 4). Such a system enables periodic irrigation of the bladder with mild antiseptic solution, thus controlling any existing infections, and only disconnected or changed under aseptic technique thus avoiding the introduction of new infection. Small doses of urinary antiseptics continuously given over long periods of time when well tolerated, further aid in controlling infection.

Drainage is maintained until either complete bladder recovery or the final neurogenic pattern has been established. This transition into the chronic neurogenic pattern is realized by cystometric examinations performed periodically.

THE MANAGEMENT OF THE CHRONIC  
NEUROGENIC BLADDER

1 The reflex neurogenic bladder which results from lesions above the conus is characterized by periodic incontinent evacuation. Its capacity of approximately 150 to 250 cubic centimeters allows satisfactory degree of comfort and continence in the patient whose intelligence allows him to adapt himself to its periodicity. Any factors which tend to increase the reflex irritability of this bladder reduce its capacity and increase the frequency of involuntary voiding. Infection and calculi are the common irritating factors and their prevention or elimination are of paramount importance in attaining the ideal status for this type of bladder. In our experience drug therapy designed to influence either the sympathetic or parasympathetic innervation of the bladder have had no clinical beneficial effect in this or any other type of neurogenic bladder.

2 The autonomous neurogenic bladder results from destruction of the conus or cauda equina, thus denervating the bladder. This bladder has no reflex activity, its intravesical pressure is high, the internal sphincter is hypertonic acting as an obstruction and the patient carries a high residual with overflow dribbling.

There are two methods of treatment. First, periodic manual suprapubic compression with straining in an effort to produce partial or complete evacuation of the bladder. When successful this method of evacuation provides reasonable relief of incontinence and is a satisfactory solution to the problem. Failure may result from too great an imbalance between the obstruction by the spastic internal sphincter and the forces available for evacuation. In this event transurethral resection of the internal sphincter may so relieve the vesical outlet obstruction as to allow satisfactory periodic evacuation as described above. We have resected a number of patients of this type with encouraging results.

Presacral neurectomy theoretically should relax the internal sphincter in these cases and facilitate manual evacuation of the bladder,

attaining the same end as sphincterotomy. Our experience with sympathectomy in this group of patients is inadequate to warrant positive conclusions.

In the event that the above methods fail to result in satisfactory periodic evacuation with urinary continence, permanent suprapubic drainage or interval catheterization are required.

3 The atonic neurogenic bladder results from interruption of the sensory components of the reflex arc. This bladder is characterized by a low intravesical pressure, a relaxed internal sphincter and a high residual urine with dribbling incontinence. There is no reflex activity, so automaticity can never be hoped for. Periodic evacuation can generally be accomplished by manual suprapubic pressure with straining. In this situation, voiding is more easily accomplished than in the autonomous bladder in which a hypertonic internal sphincter exists. Permanent suprapubic drainage is rarely necessary since periodic manual evacuation is usually successful. Presacral neurectomy should be of no value in this type of bladder because the internal sphincter is relaxed.

The ideal to be attained in any patient having a chronic neurogenic bladder is periodic evacuation of the bladder with satisfactory urinary continence and the avoidance of urinary sepsis. This ideal can be attained even under the most trying circumstances with most patients affected with traumatic myelitis. Asepsis, antisepsis, an understanding of the physiological principles involved, and infinite patience are required in order to rehabilitate this group of unhappy individuals.

## REFERENCES

- 1 LANGWORTHY, O. R., KOLB, L. C., and LEWIS, L. G. *Physiology of Micturition*. Baltimore, Md. Williams & Wilkins, 1940.
- 2 McLELLAN, F. C. *The Neurogenic Bladder*. Springfield, Ill. C. C. Thomas, 1939.
- 3 MUNRO, D. The cord bladder, definition, treatment and prognosis when associated with spinal injuries. *J. Urol.*, 1936, 36: 710.
- 4 NESBIT, R. M., and GORDON, W. G. The neurogenic bladder. *Pennsylvania M. J.*, 1940, 43: 1261.
- 5 VORIS, H. C., and LANDES, H. E. Cystometric studies in cases of neurological disease. *Arch. Neurol. & Psychiat.*, 1940, 44: 118.

# THE PRINCIPLES OF SURGERY OF THE COLON

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IT is because today the language of surgery is a universal tongue that such occasions as this should signalize a generous expression of gratitude for the culmination of those works which have at the hand of many through the golden ages of time slowly found their way into the boundless coffers of our ever increasing wealth of surgical knowledge and experience.

It is a tribute to those of the four corners of the earth who have bent the shoulder of effort to the unhurried wheel of surgical progress in the tireless solitude of unheralded study. All this because no single surgical achievement, however simple, can stand alone, separated from the past, independent, and isolated from the future, for each tiny step in the common procedure of today has a background of generations of thought and experience.

Surgery child of trauma, by necessity developed as a defensive and reparative act against the injuries of prehistoric man and animal. With the advance of civilization the demand upon the creative ingenuity of those who administer to wounds and trauma of war and industry has increased hugely.

Upon the fundamentals of traumatic surgery are based the entire field of the elective act as practiced today. Recorded first in the laborious hand of the scribes, and then in printed type are thousands of pages of history which preceded the heroic achievement of Ephraim McDowell, whereby abdominal surgery was born. Upon that memorable event whole new fields of surgical endeavor measureless to man were unfolded in a glorious panorama of the future, resplendent with the fruit of intellectual fertility burning with the vigor and enthusiasm of youth, though tempered by the judgment of ages and buttressed by centuries of industry, courage, and honesty.

In the field of surgery the thought not only of nations but even of civilizations has been woven together oblivious of time space, and

belief into a pattern which has created a universal brotherhood—a brotherhood with but one common interest, a tie far deeper than blood, far wider than race—the development and progress of surgery.

This progress has not been a steady unimpeded rise based on the simple accumulation and correlation of scientific data, but like the cultural history of mankind it has often faltered—flattered because of the blind intolerance of ignorance shrouded in the cloak of superstition and nurtured by the charlatan and the mountebank.

Hampered again by the goading decimation of plagues or the devastation and destruction of warfare, it was still further retarded by the ravages of avarice, ambition, and envy yet new milestones on the pathway of medicine continue to fade into the distance as have the footprints of the silent great who have left their everlasting mark in the pages of medical history.

In spite of turbulent periods of social conflict, economic uncertainty and political unrest, the world of science alope is at peace. The true surgeon, a scientist at heart, though suffering the sorrows and pain of existing tragedy may turn for consolation to the glories of scientific progress. Elective surgery the last born progeny of the surgical art, records among its earliest efforts operations for benign and malignant lesions of the lower segment of the alimentary canal. Surgery of the colon proper naturally was held in abeyance until the Listerian era, which followed the discovery of anesthetic agents and permitted the deliberate invasion of closed body cavities without assuming inordinate risks.

It has progressed slowly step by step from the early elementary though ingenious attempts of Hippocrates to treat fissures, fistulas, and hemorrhoids, down to such extensive operations as segmental or total colectomy the heroic one stage combined abdominoperineal resection of the rectum and other quite formidable procedures commonly practiced

today Such operations are no longer euphoric dreams of the past, but a culmination of carefully correlated results of centuries of conscientious endeavor tempered with fortitude, persistence, and ingenuity

The history of progress in this field of surgery has been punctuated with many of the great names in medicine, and to pause briefly in tribute to these sturdy pioneers is to avail ourselves of an opportunity perhaps too frequently overlooked in the turmoil of life's quickening tempo

Hippocrates, Celsus, Paul of Aegina, John of Arderne and of the Arabs, such surgeons as Avicenna, Albucasis, and Rhazes, are foremost among the pillars of progress in the early treatment of rectal disease

Morgagni, early in the eighteenth century, proposed the operative treatment of cancer of the rectum which was first attempted by Faget in 1739 However, Lisfranc is usually accredited with this achievement because of a thesis published by his pupil Pinault, who, in 1829, reported 9 cases in which Lisfranc used the perineal resection Dieffenbach and Velpeau modified this primitive procedure, while Amussat, Verneuil, Kocher, and later Kraske, developed and popularized coccygectomy and the partial removal of the sacrum for more adequate exposure

The development of surgery of the lower gastro-intestinal tract lagged behind surgery of the stomach and biliary passages for many years, perhaps without good reason, but it is a fact that the early pioneers of abdominal surgery made fewer attempts at correction of pathological lesions of the colon, instituted fewer research problems, and understood less clearly the physiology of this portion of the alimentary canal than of its fellow higher up A few hardy souls persisted steadily and doggedly, however, to extend the surgical horizon with the result that today many lesions of the colon and rectum, hitherto ignored for one reason or another or deemed unapproachable by surgery, have found remedy or palliation by operative maneuver

The development of colostomy, as a means of colonic decompression, was reported as used by veterinarians with success years before Praxagoras, in 400 B C, opened the abdomen

for ileus, incised the bowel to evacuate its contents, and then closed both bowel and abdominal wall There is no available record of the outcome of this procedure, nor is there further mention of its use until 1710 At this time Littré is said to have performed a colostomy for imperforate anus in an infant, but not until 1776 was the procedure utilized by Pillore in the treatment of cancer of the rectum Later DuBois and Duret performed colostomy for imperforate anus, but nearly a quarter of a century passed before left inguinal colostomy attained recognition in its present day usage

Baudens, Keyworth, Ward, Allingham, and others continued in this field to develop modifications of the operation for posterior resection of the rectum, and, in 1880, Czerny, attempting such a procedure found the growth well up in the rectosigmoid and was forced to remove it transperitoneally The operation was unintentional as well as unsuccessful, but the principle of the combined operation was discovered, although von Volkmann in 1889 is usually credited with having envisaged such a procedure which was later carried out by Miles with its recognized present day success

In 1823, Reybard resected the sigmoid flexure for cancer in a man of 29, and made a primary anastomosis The patient recovered but professional criticism served to discourage the popularity of so drastic a measure Again, in 1843, Thiersch resected the colon for an acute obstruction, but by 1880, 37 years later, only 10 resections of the large bowel had been recorded, of which 3 were successful

During the next 20 years, however, such names as Billroth, Marshall, Kraussold, Bloch, Mikulicz, Weir, and others are among those associated with the advancement of surgery of the colon, and to these persistent, bold, and enterprising masters, we, of the present generation of surgeons, owe a debt of homage for its modern status Today the scope of application of the operative act to many lesions of the large bowel hitherto considered ill-fitted for surgery has been enormously broadened Intractable ulcerative colitis, which has rendered the lower bowel a useless physiological organ or a distinctly harmful focus of infection, now responds favorably to total colectomy Attack on megacolon through the sym-

pathetic nervous system brings about a normal bowel function in a high percentage of cases. Operations for complications of diverticulitis are routine in application and have definitely established indications and limitations. The surgery of adenomatous coli is a favorable chapter and other pathological entities such as hyperplastic tuberculosis, fecal fistulas, benign tumors, intussusception volvulus, etc. continually appear on the surgical list in all busy surgical clinics.

The most frequent and serious lesion of the colon and rectum which engages the surgeon's attention is cancer and efforts to develop extensive, technical maneuvers for its radical extirpation and cure are continually being carefully thought out and scientifically tested.

Surgical extirpation of the growth is the only method of treatment which offers favorable prognosis. There is no other opportunity of cure albeit certain agents of palliation deserve consideration. Nevertheless, prognosis following operation, which shows 61 per cent of cases without nodal involvement and 30 per cent of cases with nodal involvement free of cancer at the end of 5 years, certainly affords opportunity for optimism. In the lowest segment of the alimentary canal the outlook is even more favorable and the average percentage of cures from the clinics of the most experienced surgeons here and abroad shows 58 per cent of patients alive and well at the end of 5 years, including both those with and without glandular involvement.

When such figures are buttressed with the favorable mortality percentage of 6 to 10 per cent and a resectability rate of approximately 75 per cent, the importance of increasing all known safety factors to insure favorable curability curves is emphasized, for the optimum of surgical treatment for any organic lesion demands a combination of these elements, and to this end offensive plans in dealing with lower intestinal malignancy have been triangularized into measures of co-operation between all professional groups concerned with both diagnostic and therapeutic measures. Safety factors of the greatest importance are (1) relief of obstruction (2) combating dehydration, desiccation and anemia by a period of pre-operative preparation (3)

local cleansing of the bowel during this period and the elimination of infection both by lavage and chemotherapy (4) evaluation of the physiological reserve of the patient based upon laboratory procedures as well as physical examination and clinical appearance (5) meticulous attention to operative detail and the adjuncts of time saving, gentleness in handling tissues, and particularly the choice and administration of anesthetics (6) vigilant postoperative care under personal supervision.

The importance of rehabilitation from depletion which results from malignant disease often superimposed upon a local septic process demands careful scrutiny of the nutritional state of the individual and attempts to combat dehydration, lowered physiological reserve, and vitamin deficiency by the administration of blood, vitamins, and high caloric diets may not be overemphasized. Rehabilitation is second in importance only to decompression and exercises a direct influence upon an operative outcome both immediate and remote.

It is necessary to mention the use of an intraperitoneal vaccine as a method of increasing resistance to infection and its influence upon operating mortality. Formerly I felt convinced that a great drop in the mortality curve was the direct result of such a practice, but in recent years since its abandonment without detriment to mortality figures, the conclusion has been forced upon me that the method of intraperitoneal vaccination which I formerly employed was not a major factor of success. Convinced nevertheless that there is a potentially sound and logical basis for its use, it is my hope that continued experimental work along this line will eliminate the present dangers of its employment and crystallize the advantages according to its use.

The whole pattern of safety and progress reflected in the hospital casualty list and in morbidity and curability graphs indicates the huge advances from the technical standpoint which have made it possible to undertake radical surgery in this portion of the intestinal tract with justifiable enthusiasm. Boldness in attack on cancer here as elsewhere is essential to ultimate success, but planning must be to the end that the patient's elements of resistance are conserved to withstand radicalness.

in execution. In consequence, while extreme methods useful to implement removal of malignancy are rewarded by low hospital death rates, it must be remembered that no radical procedure can be dissociated from a certain mortality secondary to remote complications. Increasing the safety factors has largely done away with immediate complications of operation, such as hemorrhage, leakage, obstruction, and other similar unfortunate sequelae, but the fact remains that in the majority of deaths following colonic operations the lethal factor is peritonitis which is closely followed by pulmonary complications such as embolism and bronchopneumonia.

This triad continues to harass abdominal surgeons and although energetic, untiring efforts are continually being directed toward increasing peritoneal resistance, combatting circulatory changes, and pulmonary complications, there still remains a great risk both immediate and remote to any measure which involves removal of a segment of bowel.

In all efforts aimed at the extirpation of portions of the colon, experience, often bitter and disappointing, but always in the hands of surgical thinkers offering a suitable reward for its effort, has shown immeasurable progress in the last quarter century. It has come about that recognition of a number of essential steps among which decompression, rehabilitation, graded operations, and multiple types of operations are notable has resulted in a huge reduction of mortality figures, an extension of the horizon of operability, and a roster of 3 and 5 years' freedom from malignancy which parallels the end-results of cancer therapy elsewhere in the gastrointestinal tract, if it does not surpass it. These advantages have not been attained without the necessity of recording many failures before the principles which are now routinely acceptable were firmly established.

It is within the memory of even the younger surgeons of today that resections of the stomach, resections of the colon, ablation of the thyroid gland, sudden decompression of the urinary bladder, and prostatectomy were undertaken with little, if any attention, to preliminary preparatory decompression and resuscitation, in part or in whole, of physiological

equilibrium. Aside from technical maneuvers which applied either in one or multiple stages have avoided many pitfalls of surgery inviting infection, the one principle of decompression perhaps has resulted in saving more lives than any single step in surgery for abdominal cancer. No longer is it justifiable, indeed, it is distinctly culpable to subject to a major procedure for a chronic ailment, an individual whose ability to resist surgical invasion has not been evaluated by careful estimates of the physiological functions of his several vital systems. In dealing with cancer of the colon the necessity of emptying the bowel of its content, of allowing time for the hypertrophied and dilated gut wall to return to normal and simultaneously to reduce infection around the local lesion is so obvious as to be beyond the stage of debate. Most cancers of the left colon and the rectosigmoid juncture produce some degree of obstruction at some time during their existence. Who has not had the experience of exploring an abdomen harboring a colonic cancer with complete confidence that the bowel was adequately emptied only to find on viewing the local growth telangiectases prominent on the proximal gut, edema in the tissues of the mesentery, thickening of the entire bowel wall, a few enlarged glands adjacent to the growth, and other evidences of obstruction? The very nature of many growths especially the encircling type so common in the left colon, predisposes to luminal stenosis. Further around in the right half of the large bowel, which is the physiological portion of the lower gastrointestinal tract developed with and functioning as the small bowel does, one finds less tendency to obstruction but more often evidences of physiological imbalance. With local signs demanding decompression and rehabilitation, with laboratory evidences of failing cardiac capacity, a lowered renal function, and general physiological regression, one no longer questions the advantage of a preliminary period to combat physiological imbalance, to empty the lower gastro-intestinal tract, and to reduce local obstruction by adequate decompressive measures. Meticulous pre-operative measures are carried out as one phase of a surgical offensive supplemented by accurate, painstaking, and careful operative

maneuvers which in turn owe their selection to mature surgical judgment and are followed by a watchful postoperative care.

The immense advantage in operating upon many cancers of the colon and rectum by multiple procedures is recognized by all surgeons. It is probably a good plan for surgeons not particularly trained or interested in surgery of the lower gastro-intestinal tract to utilize graded operations more often than otherwise. Nevertheless, with increasing experience, better selection of cases, and more accurate preparatory programs, one finds the trend indubitably toward single maneuvers for cancer of the rectum and in many instances for cancer of the colon as well.

The selection of operation and the choice of single or graded operation obviously is such an important safety factor that each case must be individualized, the gravity of the situation to each patient evaluated, and the operation fitted to the patient rather than the reverse.

The paramount issue in approaching an operation for resection of a segment of bowel is one of obstruction. As Tiffany quaintly remarked, "Resection in the face of obstruction is fatal, and increasing experience lends credence to his theme."

Modern surgery of the colon and rectum represents a sound practical attack on pathology based on a foundation of physiology which has been established by both experimental data and clinical observation. With the huge advance in pathological gradings, with the accuracy of diagnosis now routine in the hands of competent roentgenologists and proctologists, and with a large group of surgeons trained in the management of these cases, it is not strange that proper indication for operation and proper application of technical procedure to individual cases has broadened this field of surgery immeasurably.

In selecting a type of operation for removal of malignancy of the lower gastro-intestinal tract the principle of radical resection of not only the growth and the tissues immediately in juxtaposition but also the lymph-gland bearing tissues more distantly situated must be adhered to. In the colon itself the majority of its segments are supplied with blood through a relatively long flexible mobile mesentery

which likewise houses the lymphatic system.

In the cecum, however, only about 20 per cent of the cases show a fully developed mesentery. The splenic flexure similarly is usually more or less fixed as is the portion below the rectosigmoid juncture. These areas, except for the splenic flexure, however, are richly supplied with lymphatics which are favorable to migration of malignant cells. These glands must be removed in any plan which is to be followed by a large number of long time survivals. The importance of removing gland bearing tissues distant from the original growth is recognized in dealing with cancer elsewhere and it is no less necessary to extirpate wide areas of mesentery in removing a colonic cancer than it is to do an extensive dissection of the axilla as a routine in operations for breast cancers or to apply the principles of dissection en bloc in orolabial malignancy.

The work of David and Gilchrist, published in 1938 and more recently supported by statistics from St. Mark's Hospital, London, demonstrates beyond peradventure the necessity of widespread tissue removal in cancer of the rectum. They showed that, in 68 per cent of resected rectal cancer specimens, glandular metastases could be demonstrated by a painstaking examination of a large number of glands. What further proof is necessary to demonstrate the desirability of removal of a large portion of sigmoidal mesentery in dealing with rectal cancers?

It is futile to assert that it is impossible to do a gland dissection of the pelvis. Miles' beautiful demonstration of rectal lymphatics has established the fact that the majority of metastases take place in the upward zone of spread, namely toward the sigmoid, and by his type of operation gland bearing tissues for rectosigmoidal and ampullary cancers are removed satisfactorily in the majority of cases.

In this connection it is permissible, I trust, to support the thesis that radical operations for removal of rectal cancers which carry out these established principles must furthermore include, as one of the technical details, the manufacture of an artificial stoma. This step necessitates the sacrifice of the splendid sphincteric mechanism of nature—a sacrifice which

the layman is always loathe to endure and one which many physicians are apparently reticent to recommend. It is true that any mutilating operation is a most unpleasant duty to perform, yet, in dealing with cancer, destructive and mutilating methods which may be proved statistically to save lives in a larger percentage of patients than less radical measures must be accepted.

The dislike of a colostomy is a state of mind which may readily be overcome by a sympathetic attitude to it, and in supplement a properly constructed stoma. Its possession entails no social ostracism and frequently but little interference with professional and social activities. The decision evidenced occasionally by surgeons to co-operate with the desire of the patient to save the sphincteric mechanism will be readily abated by a careful perusal of factual analyses, for operations which violate surgical principles are not followed by uniform success.

I would not be understood as condemning totally the employment of procedures for saving the rectal sphincters. I would even concede that in a low grade growth which has not metastasized, in many instances the operation may be useful. It would be interesting, however, and instructive to have criteria established which would permit us to tell without resection which cancers were still local and which ones had metastasized.

In removing segments of the colon, widespread resection of its mesentery is not difficult. The more important decision comes, first, between graded procedure or single stage procedure, and second, between immediate reestablishment of the gastro-intestinal continuity and delayed union.

Graded procedures, advantageous as they are, may be abandoned when an estimate of the patient's general ability to withstand a formidable intraperitoneal operation permits and the local conditions are satisfactory. Local conditions which influence the use of multiple maneuvers are (1) fixation, (2) infection, (3) obstruction.

It is a well known fact definitely established by experimental and clinical research that the combination of obstruction and ulceration increases the permeability of the intestinal wall

and permits the migration of organisms into the pericolic tissues. Under condition of fixation the very act of mobilization encourages peritoneal contamination. However, in a sturdy risk in whom the growth is free and not firmly held to the lateral parietal peritoneum, and in whom the obstruction has been relieved by preliminary preparatory measures, one may, with confidence, employ a single stage maneuver of anastomosis and resection.

One may not easily overestimate the advantages of a complementary decompressive measure in the event one selects a single stage resection in either the right or the left segment of the colon. Whether one employs open anastomosis or aseptic anastomosis, the healing power is diminished in a cancer patient, particularly if the growth is in the right colon and is accompanied by the usual profound anemia without visible loss of blood. In consequence, about the third to the fifth day during the "lag-period" of healing, increased intraluminal pressure may compromise the suture line. This may be avoided by the use of a complementary ileostomy at the time of resection or the introduction of the Miller-Abbott tube after resection, as advocated by Whipple.

What method of suture is employed is largely a personal equation and arbitrary pronouncements, relative to the advantages of one type of suture or one type of anastomosis, are rarely fundamentally sound nor do they always reflect mature judgment.

As an advocate of aseptic anastomosis, I believe it is more desirable because it diminishes if it does not abolish the element of infection, and experience has shown that it may be accomplished with ease and satisfaction in the hands of most surgeons. At the same time it would be extremely dogmatic to urge that any single operative method to accomplish an objective so far outbalanced the disadvantages of all others as to make it indispensable. Elements of personality and circumstance must inevitably influence the choice of technique, and in consequence, the range of maneuvers continues wide and at the same time acceptable so long as fundamental principles are observed. The utilization of absorbable or non-absorbable materials likewise is more a matter of personal choice than of grave impor-



tance. The colon heals readily when it is approximated by suture to the small bowel for the blood supply of the latter is copious and plentiful. When joined segment to segment in its own continuity it likewise heals with relative kindness for the blood supply of the colon, although less plentiful than that of the small bowel is nevertheless of a constant pattern and adequate. The occasional leakage from efforts immediately to anastomose the colon is the result more often of infection at the suture line than it is of failure of the blood supply. True, failure of the blood supply secondary to infection and thrombosis accounts for a number of cases, but by and large vascularization to the cut ends of the bowel may be demonstrated by visual inspection.

For this reason it is comparatively easy to agree with those who advocate immediate anastomosis by suture in selected cases, always provided that a cecostomy has either preceded the resection or accompanies it as a complementary measure.

There are certain safety factors inherent to a delayed type of union which have proved not undesirable. Obstructive resection plus complementary cecostomy is an example of the operative act which accomplishes a radical removal of the growth and gland bearing segment of the mesentery without subjecting the patient to many of the hazards of immediate re-establishment of continuity by suture. The subsequent removal of the spur by pressure necrosis and healing of the wound completes a method which is accomplished with such a low mortality that it has appealed to me as a safe and satisfactory type of operation to be used in the majority of cases of cancer of the colon situated beyond the middle of the transverse colon.

It is difficult to agree with the opinion that the time element involved in this type of operation makes it less satisfactory than other procedures which carry a greater risk yet cut down the morbidity figures, for to integrate economic conditions with surgical judgment must surely lead to controversy.

In support of this thesis it may be pointed out that probably the greatest single technical factor in advancing colonic surgery was the discovery of the principle of exteriorization.

In the early nineties, it was found that a segment of bowel could be extraperitonealized, the abdominal wall closed snugly around it, and the removal of the tumor bearing loop postponed until nature had agglutinated wound surfaces and sealed off the peritoneal cavity. This discovery marked an epoch in colonic surgery by which mortality was hugely decreased and a great impetus given to a field of surgery hitherto granted frugal recognition by the medical world. Many names are associated with this type of operation, but it seems definitely established that Bloch, of Copenhagen, deserves credit for the first account of the principle published in 1891. In 1892 Redcluse collaborating with Forgue published a description of 2 cases of exteriorization of the bowel without mentioning Bloch's name. Paul, of Liverpool, 9 years later in 1900, published a modification of Bloch's method, ligating the mesocolon, abutting the two loops of bowel and decompressing the proximal loop by insertion of a glass tube. In 1902 Mikulicz, in the *Transactions of the Thirty-second Congress of German Surgeons* spoke of the procedure which he alleged he had performed first in 1885. The operation so commonly referred to in this country as the Mikulicz operation represents as it is so often the case the concepts of many surgeons, for discovery of a principle rarely comes as an isolated procedure, and more rarely as the work of one man. Multiple experiences, discussions, and researches combine to eliminate false impressions and establish truths in the birth of any principle, and so it is with exteriorization which is an ensemble of principles marking a new era in surgery of the large bowel. With its advent, danger of resection was largely reduced, leakage at the suture line was abolished and utilization of the fact that nature's reparative processes by agglutination of approximated peritoneal surfaces were adequate immediately popularized the method. As with all new methods there ensued a period in which its application, little understood, resulted in the customary abuse of a very new technique. Controversy early developed and still remains as to the desirability of ligating the blood supply in the mesentery of the bowel and bringing out a longer more mobile loop. This step entails a certain

amount of danger, for necrosis and ulceration occasionally result in leakage into the peritoneal cavity, and death. Certain anatomical types make the bowel impossible of exteriorization, and a short mesentery filled with fat and inflammatory reaction becomes a distinct contra-indication.

With increasing experience at the hands of many surgeons both in this country and abroad, the definite limitations and indications of this procedure have been recognized and its place in the armamentarium of the modern operator firmly established. With the impetus given to surgery of the colon by the reduced mortality accompanying exteriorization, many other procedures were evolved for extirpation of cancers of the right and left halves of the colon in single, double, and even triple stages.

The ultimate aim of all types of operation for cancer is cure, but it must be recognized that there is a definite group of cases in which cure being impossible, the ingenuity and resourcefulness of the surgeon may still be available in the application of palliative procedures. Such a decision, often difficult in the extreme, is a function which no surgeon may escape, for trying as it is, it demands a not inconsiderable amount of courage as well as superb surgical judgment. One must often decide whether resection as a palliative measure is justifiable or whether because obstruction is not present the abdomen is closed and the individual permitted to languish agonizingly from multiple metastases and the ultimate lethal sequelae of carcinoma. It is a not uncommon experience to explore a patient with a cancer of the colon which is freely movable, and resectable with a reasonable mortality risk, and to find by palpation of the liver surfaces multiple umbilicated, irregular, malignant nodules. Removal of the local growth, precluding obstruction, fixation to neurogenic elements, and other painful complications, is often warranted under such circumstances, even though the mortality figures may be higher than in more hopeful cases. Death from cancer of the liver is a not too painful experience and in such circumstances, removal of the primary growth and consequent comfortable prolongation of life, is entirely praise-

worthy. When obstruction has supervened with fixation, abscess formation, or other local complications with or without metastasis, drainage procedures either by bringing the alvine discharges to the outside through colostomy, or by-passing them by entero-anastomosis, give comfort and relief from the distressing period of impending dissolution.

The realm of palliative surgery has been somewhat overshadowed by the emphasis placed upon curative procedures, but in the treatment of neoplastic disease one cannot submerge the humanitarian interest in order to effect a surgical masterpiece of technical perfection, while the sufferer is offered no relief because he fails to comply with the rigid postulates of the curative endeavor.

The progress of scientific endeavor has during the last century done more to relieve suffering, to improve health, and to prolong life, than has been done during the entire span of civilization up to this time. It is because of this ever accumulating wealth of knowledge that the effort of intensive concentration has been father to specialization. In consequence, surgery of the colon and rectum has proved worthy of high rank in the surgical domain, for accomplishment has reached heights far beyond the fondest expectation of those tireless workers who laid the corner stone in the temple of our guild.

If, however, further discoveries in biochemistry and allied sciences displace surgery in the treatment of cancer, and as Dabney puts it, "cancer is ever shown to be a systemic disease, the technical literature on the radical removal of malignant lesions may become as obsolete as that of pouring burning oil into wounds," still the record of these operative maneuvers will remain as a monument to the persistent effort, skill, and ingenuity of surgeons of the past and present generation, and their vast achievements will continue to live in the glorious realm of tradition.

Complex problems both of physiology and pathology and changing trends in treatment testify that surgery in this field has not reached its ultimate, despite the well known tendency of great surgeons, consummating a meritorious career to deplore the fact that "there are no new worlds to conquer." From Paré, Vel-

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peau, Moynihan, and other masters, such laurels have come, yet strangely enough after each declaration some new discovery in surgery has been announced. Surgery of the colon is no exception and new advances in this field, limitless in opportunity will continue to

crown the endeavors of those who strive zealously and with the energy, ambition, and intelligence characteristic of the progressive minds who have planted markers of surgical discovery and who have written chapters in medical history

## HEPARIN IN THROMBOSIS AND BLOOD VESSEL SURGERY

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THE experimental proof that heparin would prevent thrombosis opened a field for a progressive advance in the surgery of diseases and obstruction of blood vessels. The important discovery of heparin by Jay McLean in Howell's laboratory was the first step in providing a substance which would prevent thrombosis and allow of certain operations which otherwise were doomed to failure because of recurring thrombosis at the site of operation. The final purification of the substance by Best, and Charles and Scott thereby provided a substance which was non-toxic, and placed it on a footing so that it could be used clinically.

The proof of the effectiveness of heparin to prevent thrombosis was obtained when it was shown that heparin would prevent experimental thrombosis in veins (4) thrombosis at the site of arterial anastomosis, and also thrombosis in venous grafts in an arterial tree. It was shown also that it would prevent recurring thrombosis at the site from which an experimental embolus had been removed and its effect in preventing thrombosis in the portal system was also demonstrated.

These experimental facts demonstrated the possibility of this substance being used in clinical cases in which repair of injured important arterial and venous trunks would be an advantage extensive venous or arterial thrombosis was occurring embolic occlusion of main peripheral arteries had occurred or in which thrombosis of portal vessels was a factor such

as following splenectomy or following resection for mesentery thrombosis. Its use in diseases in which there is extensive thrombosis, such as in osteomyelitis and coronary artery thrombosis, has not been thoroughly investigated but warrants some investigation.

With a purified nontoxic preparation of heparin available, my associates (3) and I began administering it to clinical patients. It had been given clinically to prevent clotting in blood transfusions by Mason and McClure (5) but it produced toxic effects and did not come widely into use clinically. To date about 700 of our patients have been treated with heparin in sufficient doses to raise the clotting time to two or three times the normal level. Except for a few months in 1939 when there were definite thermal reactions in about 50 per cent of the patients receiving it there have been no toxic effects. The patients experience no sensations whatever as a result of the heparin administration no more than the effect of an ordinary intravenous saline. The chief disadvantage of treatment with heparin is that it is necessary for the patient to be in bed to receive the continuous intravenous injection. The effect of heparin is so evanescent (the clotting time of a patient will return from 15 minutes to normal within an hour after the injection has stopped) that it must be administered continuously. Unfortunately intermittent injections two or three times a day are impracticable because to make the effect of heparin last a few hours, so much must be given that the clotting time is elevated to several hours which, of course, is undesirable and might be dangerous.

There are no contra-indications to giving heparin except in the case of a patient who has active bleeding from an open vessel, when the prolonged clotting time will encourage the bleeding to continue. The indications for heparin are in conditions in which it is desirable to prevent thrombosis in vessels or to prevent extension of an already existing thrombus. This, of course, applies to many medical diseases and to many patients following operations. Its administration is specifically indicated if the operation has involved a direct attack on blood vessels, such as opening a lumen, or under conditions in which suture, repair, or grafting of a blood vessel is necessary.

Heparin has been used with satisfactory results in the cases presented herewith. While many of these operations might be undertaken and results might be successful without the use of heparin, still with its use, success is insured and the results have been most satisfactory.

#### ARTERIAL SUTURE

End-to-end suture of arteries has been done successfully in several cases and the circulation and pulsation have been maintained in the periphery. Three only of these cases will be cited.

**CASE 1.** A man, aged 60 years, while using a hammer, had a piece of steel enter the upper arm about  $2\frac{1}{2}$  inches above the elbow. Immediately there was violent hemorrhage. When this was controlled a large swelling developed in the arm and this was accompanied by severe pain over the distribution of the median nerve. Clinical examination within 3 weeks demonstrated a mass with expansile pulsation and with a bruit over it. It was obvious that this was an aneurism of the brachial artery with pressure on the median nerve. The circulation to the extremity was normal although the pulsation in the radial and ulnar arteries at the wrist was very feeble. The median nerve pain was so severe that the patient asked to have his arm amputated and for this reason it was decided to operate upon this swelling at an early stage. The brachial artery was found divided about half way across. This opening communicated with a false aneurism about 2 inches in diameter. The aneurism was removed. The rent in the artery was of such a size and shape and with thickened friable margins that it was unsuitable for suture. Therefore, it was decided to divide the artery across and trim off the ends. By moderate flexion of the elbow, the divided ends were easily brought into apposition when an end-to-end anastomosis with a continuous fine silk suture was car-

ried out without difficulty. Heparin was injected to fill the vessel at the site of the anastomosis. Immediately following the restoration of circulation normal pulsation returned in the vessels of the wrist. A continuous intravenous injection of heparin was given for the next 3 days keeping the patient's clotting time at about 15 minutes. The circulation remained normal in the extremity. The median nerve pain disappeared and the patient returned to his work as a laborer 4 weeks after the operation.

**CASE 2.** This patient, as the result of a motor car accident, had the brachial artery torn completely across about  $1\frac{1}{2}$  inches above its bifurcation. The patient, was seen several hours following the accident. The arm was greatly swollen, and with its change in color, loss of sensation and motion, with loss of pulsation at the wrist and loss of heat, it obviously was in a pregangrenous condition. At operation the ends of the artery were found separated by about  $1\frac{1}{2}$  inches and both ends were plugged with blood clot. The clots were removed. The ends of the vessels were trimmed and with a continuous silk suture a satisfactory end-to-end anastomosis was carried out. The patient returned to his work as a garage mechanic 6 weeks following his operation. He has been able to continue at his work for more than 2 years with a hand which is normal in all respects.

**CASE 3.** During a neck operation an excellent surgeon had the misfortune to damage a common carotid artery dividing it across completely. About  $\frac{3}{4}$  inch of the length of the artery was resected to remove the damaged portion of the vessel. By flexion and lateral bending of the neck the ends were brought into apposition and a satisfactory end-to-end anastomosis was completed. This restored the circulation as indicated by a normal pulsation distal to the site of the anastomosis. Heparin was injected continuously over the next 8 days. The circulation was maintained through the artery and the patient had no ill effects in the way of cerebral symptoms, either from anemia or embolism, as might be expected to occur in up to 25 per cent of such cases had the artery been ligatured.

#### ARTERIOVENOUS FISTULA

While arteriovenous fistula may be treated surgically in a variety of ways, it is now possible with the use of heparin to resect and repair the vessels satisfactorily if this seems desirable. This has been carried out on several occasions.

**CASE 1.** A bullet wound in Scarpa's triangle had produced two arteriovenous aneurisms between the superficial and deep femoral arteries and their corresponding veins. The damaged segments of the vessels with the aneurismal sacs were removed and the vessel reconstructed satisfactorily and heparin administered intravenously. The circulation and

pulsation in the extremity has remained normal since that time now  $\frac{1}{2}$  years since the operation.

Two other such fistulas of blood vessels have been removed and the vessels repaired thus restoring normal circulation to the extremities.

#### VENOUS GRAFTS

When segments of major arterial trunks have been destroyed by accident or pathological lesions, the usual procedure is to tie the vessels involved. Attempts have been made to bridge gaps in important vessels, but from the cases recorded the results have not been satisfactory because of thrombosis causing occlusion of the involved area. At many points large vessels may be tied without danger but in such vessels as the internal carotid major vessels of the extremities, and the aorta, disaster is apt to follow their ligation. It was with great satisfaction, therefore, that aided by the use of heparin we have been able to place venous grafts to bridge gaps in important arteries on 4 occasions. In 3 of these the circulation was restored and maintained perfectly. In the fourth because of gas gangrene in the extremity resulting from the accident, amputation was required.

**CASE** A popliteal aneurism, rapidly enlarging and about 1 $\frac{1}{2}$  burnt through the skin, caused the patient to have severe pain. It was obvious that some relief was needed urgently so at operation the aneurism was resected. This left a gap of  $\frac{3}{4}$  inches in the popliteal artery. The remaining segments of the artery were greatly dilated and the walls were thickened and calcareous. While ligation of both ends of the vessel might have given satisfactory result, the danger of gangrene from ligation of the popliteal artery was also considered. It seemed that this was suitable case in which to attempt a popliteal venous graft. The external jugular vein was removed and the gap of  $\frac{3}{4}$  inches was satisfactorily bridged by double end-to-end suture of the graft to the segments of the artery. There was considerable difficulty in matching the small size of the vein to the larger size of the artery. This caused considerable stretching especially where the greatly dilated proximal segment of the artery necessitated great stretching of the vein to complete the anastomosis. Following the injection of heparin, the circulation was restored with normal pulsation appearing in the vessels of the foot. The circulation remained normal in the foot for  $\frac{1}{2}$  weeks. At this time there was sudden recurrence of pain in the popliteal space. On examination there was pulsation of mass and bruit which could be heard with

stethoscope. It was obvious that another aneurism had formed. The area was again explored. It was found that the circulation was still being carried on through the graft. Its wall was thicker and the lumen was greater than when it was applied  $\frac{1}{2}$  weeks previously. These changes corresponded to those which were demonstrated in the experimental venous grafts. Just distal to the proximal suture line the anterior wall of the venous graft, where it was unsupported by living tissue, was running across a large cavity in the popliteal space, had given way and a small false aneurism had formed. On exploring through this opening it was demonstrated with probe that the lumen of the graft was patent and that there was no stenosis at the suture lines. In spite of the urge to recover the specimen, it was decided to repair the aneurism of the venous graft. Flaps were cut in such fashion that the lumen of the vessel was maintained and the aneurism was repaired. More heparin was injected and following restoration of the circulation there was excellent pulsation in the graft and the distal segments of the artery. The circulation has remained normal for more than 2 years, and the patient has been able to return to his work.

This was a most instructive case as it demonstrated the possibility of using a venous graft in an artery in a human being. It showed that when the patient is treated with heparin the graft survives. It does not become occluded or stenosed. Its lumen increases in diameter and its wall becomes thickened and such a graft can maintain a circulation in a major arterial branch for a period of at least 2 years.

**CASE** A young man had the misfortune to divide the femoral artery with pen knife. By prompt surgical intervention by an excellent surgeon he died off the vessel, the violent hemorrhage stopped, and with transfusions the patient survived. Within 48 hours there was some doubt if the extremity could survive. At this time he was operated upon by me. When the damaged ends of the divided femoral artery and vein were removed, there was a gap of  $\frac{1}{2}$  inches in the artery and a smaller one in the vein. It was impossible to bring the ends into position by any position of the knee or hip. For that reason segment of the adjacent vein which was already tied off was removed. The vein was turned inside out and the valve cusps removed. With this 3 inch piece of vein the gap in the artery was bridged successfully and heparin was injected. When the circulation was restored, excellent pulsation appeared in the vessels of the foot. Heparin was injected continuously for the next 8 days and then stopped. The pulsation of the vessels at the ankle was recorded every hour during this time. It did not decrease or change throughout this

time and has persisted, and the circulation of the extremity has been normal since the operation 4 months ago. The patient began walking about in 3 weeks and has been quite active since that time. There has been no aneurysmal dilatation of the graft and normal pulsation can be felt quite readily in the upper part of Scarpa's triangle. There is a slight bruit over the graft but this is not changing. There is no atrophy of the extremity and sensation and motor power are normal.

**CASE 3** A patient, aged 72 years, had a direct injury over the base of Scarpa's triangle. Immediately following this a large hematoma developed in Scarpa's triangle which extended through beneath Poupart's ligament into the iliac fossa. This was obviously a false aneurism. The lump was enlarging rapidly and it was obvious that it was about to burst through the skin. It was operated upon, and the common femoral artery just below Poupart's ligament was found fractured across. The ends were thick, calcareous, and extremely brittle, these were trimmed back until fairly normal vessel wall was obtained. This left a gap of  $4\frac{1}{2}$  inches. The adjacent femoral vein was completely occluded by thrombus, the extremities of which could not be reached through the incision. A segment of this vein  $4\frac{1}{2}$  inches in length was removed. The thrombus in its lumen was very adherent to the wall so that it was necessary to turn the vein inside out and scrape the intima to clear it of thrombus. The cusps of a valve were clipped off so the thrombus could be removed from beneath them. This left a roughened, shaggy intimal surface. The vein was turned right side out again and with a double end-to-end suture the gap in the artery was bridged. Heparin was injected and the clotting time of the patient was kept at a level of about 15 minutes. The circulation and pulsation in the vessels of the foot were normal. Within a few days the patient died of a cerebral vascular accident, and the specimen was recovered from the thigh. This showed healing of the suture lines with healing of the roughened intima of the venous graft so that it was smooth and shining. There was no clot or thrombus at any point in the venous graft, at the suture lines, or in the adjacent segments of the artery.

This was a very severe test of the effectiveness of heparin in preventing thrombosis. From the excellent result, with healing and return to normal of the wall of the venous graft, more evidence is provided that a clotting time of 15 minutes produced by heparin is quite adequate under the most unfavorable conditions.

#### EMBOLECTOMY

This operation has been questioned in recent years by physicians and surgeons alike, because of the high incidence of thrombosis at the operative site, following the removal of

an embolus. This is much more apt to happen if the operation is undertaken more than 10 or 12 hours following the occurrence of the embolism. With the use of heparin, however, the picture has been entirely changed. With the use of this substance, the operation may be undertaken successfully up to 24 hours following the accident and if the vascular tree has been completely cleared of obstructing clot and thrombus and with the proper administration of heparin, the wall of the vessel will heal without further thrombosis and the circulation and pulsation in the extremity can be maintained.

Seventeen arterial embolectomies have been done and heparin used postoperatively. In this group the circulation was completely cleared of obstruction and the circulation and pulsation at the extremities remained normal in all.

In 2 of these patients the bifurcation of the aorta was completely obstructed by a massive embolus. This was removed successfully in both cases, the circulation and pulsation was restored successfully, and both patients made excellent recoveries from the operations.

With embolisms occurring in the vessels of the extremities, the operation is a relatively minor one and can be done quite successfully under local anesthesia. With the administration of heparin, the certainty of good results is insured. It is advocated, therefore, that the embolus be removed early and the patient be treated with heparin, rather than that the patient be allowed to continue to suffer and at the same time to face the dangers and disabilities of impaired circulation in most cases, and gangrene in some.

#### MESENTERIC THROMBOSIS

Every operating surgeon is aware of the extremely high mortality in cases developing mesenteric thrombosis. With the use of heparin if started at or immediately following the operation, the prospects of recovery are very greatly improved. Six patients of this type, in all of whom resection of intestine was necessary, were treated with heparin following operation. Four of these survived and are still alive and well now more than 2 years after their operations. Two of the patients died of



other lesions but in neither of these was there extension of thrombosis in the portal system which is the usual course following operation for this disease.

#### THROMBOPHLEBITIS, PHLEBOTHROMBOSIS AND PULMONARY EMBOLISM

The prolonged morbidity with the discomfort and permanent disability following this disease lead one to try using heparin in these cases. It has been interesting to see the results of treatment in more than 125 patients. During the early acute phase of the disease the pain and aching is improved within a few hours and usually has mostly disappeared between 24 and 48 hours. The temperature, swelling, and tenderness also show improvement within the same period. In this group of cases the patients were treated for periods varying between 4 and 8 days at which time the patients were going about actively and were discharged from hospital. While it is difficult to arrive at the truth one is impressed that there is less residual edema of the legs when the patient has been treated with heparin than in corresponding cases in which patients have been treated by other methods.

When pulmonary embolism has occurred and the patient has survived long enough to have heparin administered intravenously there has been striking clinical improvement. While there is no reason that further embolisms should not occur in these patients, as heparin will not dissolve or remove clots or thrombi still in 46 cases of this nature this accident has not occurred except possibly in 2 patients who might have had further small embolisms. However this was not proved, and the patients recovered. The 44 other patients had no further attacks of embolism and showed rapid clinical improvement.

This experimental and clinical work was carried out in collaboration with Professor C. H. Best, Miss Ogata, M. L. Jansen, Dr. R. W. Johnson, Dr. F. Purdy, Dr. Ross MacKenzie, and Dr. J. Jones assisted during various stages of this work. Assistance from The Bunting Research Foundation, Commonwealth Laboratories and Mr. J. S. McLean in providing facilities and material to help carry on this work is gratefully acknowledged.

#### REFERENCES

- CHARLES, A. F. and SCOTT, D. A. The preparation of heparin from beef lung. *T. Roy. Soc. Canada*, 36, 197, 194, 281, 55.
- MASON, E. C. Not on the use of heparin in blood transfusion. *Arch. Surg.*, 64, 70, 403.
- MORRIS, GORDON. Heparin in surgical treatment of blood vessels. *Arch. Surg.*, 64, 401, 307-315.
- MORRIS, GORDON D. W. and BEST, CHARLES H. The use of heparin in thrombosis. *Ann. Surg.*, 61, 101, 163.

# SYMPOSIUM ON CANCER

## THE PRESENT STATUS OF CARCINOGENS AND HORMONES IN CANCER RESEARCH

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**I**N a previous communication the status of our knowledge concerning the etiology of cancer was reviewed (93). The rôle of the inciting carcinogenic factors including the hormones was presented from the experimental and clinical evidence as of that date. Since that time, there has been a marked increase in the number of investigations directed at these problems, now partly interrupted by the advent of the second World War.

It was but natural that the first enthusiasm of the research worker was to produce cancer in many forms and in many species with the new tools which served as inciting agents. The purified chemicals offered an easy weapon to produce carcinoma at will. The chemists industriously turned out new chemical combinations, changing their organic compounds by almost magic manipulations. The biologists then tested these agents for their cancer inciting qualities. It soon became evident that this type of research could proceed indefinitely. The emphasis accordingly shifted to the mechanism by which these carcinogenic agents brought about the process which is cancer.

In this paper, the more recent developments in the field of the carcinogenic agents, including the hormones, will be reviewed. Emphasis will be placed especially on the chemical carcinogens, light effects, and the hormones. The viruses will be considered only when they offer some fact bearing on the general problems. They constitute an important but complicated study in their own right.

Excellent reviews on chemical compounds as carcinogenic agents have been written by Cook and Kennaway (23, 24), Cook (22), and Fieser (41).

The most important cancer producing constituent of coal tar is 3,4-benzpyrene. It is insoluble in water or aqueous salt solution, but is

soluble in the serum of animals, especially fat fed ones. It probably enters the cell by dissolving in the cell lipoids. It is found only in the higher fractions of coal tar because of its high boiling point. Convincing evidence that this hydrocarbon is concerned in the etiology of human cancer has not been produced. The possibility of lung cancer arising from some such agent in motor exhaust fumes, road tar dust, etc., has been investigated without definite proof of such an origin.

Methylcholanthrene can be obtained from cholic acid, the chief acid of human bile (Fieser and Newman, 42). For this reason it seemed more likely as a possible etiological agent in human cancer. It has been shown to have a very considerable potency as an inducer of malignant tumors in rats and mice.

It is true that 1,2,5,6-dibenzanthracene is more soluble in serum than 3,4-benzpyrene. It has been less effective as a carcinogenic agent in rats and mice than the two other aforementioned chemicals. The average time for the induction of tumors has been considerably longer as well.

The three carcinogenic chemicals named have been used in various vehicles such as lard, olive oil, paraffin, cholesterol, benzene, or alcohol. They are insoluble or but sparingly soluble in most of these reagents. Colloidal solutions also have been employed. Often the crystals of the carcinogenic hydrocarbons may be found in the subcutaneous tissues at the end of the experiment. The difficulty of distinguishing a tumor growth from the vehicle carrying the carcinogen has been considerable at times.

Both carcinomas and sarcomas have been induced by all three of these carcinogens in rats and mice by epithelial painting and by subcutaneous injection. In general, sarcomas in mice have been brought out more quickly than epitheliomas. Sarcomas in rats have been induced in about the same time as epithelial tumors in mice. The latent period between the application of the chemical and the appearance of the tumor has varied with the strain, the sex, the vehicle, the dosage of chemical, and the tissue involved. Apparently

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these carcinogenic hydrocarbons have been able to induce squamous cell carcinomas from any epithelium possessing such latent potentialities. In addition to the usual cancers of the skin and spindle cell sarcomas of the subcutaneous tissues, squamous cell carcinomas and sarcomas of the prostate have been induced in rats by benzo(a)pyrene (91) hypophyseal tumors in rats by the same agent (106) squamous cell cancers of the stomach in mice fed benzo(a)pyrene by mouth (45, 8, 144) osteosarcoma in a mouse by benzo(a)pyrene (13) tumors of the lung (131) from intratracheal injections of methylcholanthrene or 1,2,5,6-dibenzanthracene, tumors in the esophagus and peritracheal tissues from methylcholanthrene (140) tumors of the brains of rats (145) and mice (128). Nikod and Regumey called attention to the exaggerated sensibility of the connective tissue to methylcholanthrene and benzo(a)pyrene. They were unable to produce tumors of the parenchyma of organs which were injected with these substances because of the fact that the connective tissues gave sarcomas first in each instance.

In mice of known genetic constitution, C 57 brown, Miller and Morton (83) noted the remarkable fact that occasionally benign and malignant epitheliomas followed a single painting with methylcholanthrene. The usual sequence for such events has been a long continued repeated application of the carcinogen. The same investigators (89, 90) have been able to show a marked reduction in the latent period for spontaneous lymphomatosis and spontaneous mammary carcinomas in the dilute brown mice of Little, when they were painted repeatedly with methylcholanthrene. Apparently these carcinogens can bring out the latent potentialities of the tissues of the tested animals for tumor formation. Hence, the importance of knowing the biology of the strain under investigation for a proper interpretation of the carcinogenic properties of the chemical.

The smallest dose of 1,2,5,6-dibenzanthracene known to induce tumors has been determined by Dobrovolskaja Zavadskaja (33). Single doses of 0.01 milligram, 0.005 milligram, and 0.0005 milligram were injected subcutaneously. Tumors appeared with the first two groups but not with the third.

By using different dosages of methylcholanthrene in different methods of application, Ma honey and Morton have been able to bring out several different tumor types (lymphomas, cancers of breast, lung tumors) in mice of the dilute brown strain, subline 2.

Cottini and Maxzone tested the effect of repeated applications of 3,4-benzopyrene to the human skin. Daily applications of a 1 per cent solution in benzol for periods not exceeding 4 months resulted in definite manifestations localized to the treated areas. Erythema, pigmentation, desquamation, the formation of verrucae, and infiltration developed in chronological order. Upon suspension of the applications there was complete regression of the lesions within 2 or 3 months. These changes are believed to have been the early stages of a process which would have gone on to neoplastic proliferation ultimately had the applications been continued. The alterations were more pronounced in the older than in the younger individuals and more so upon the unprotected skin surfaces.

Cook and the Kennaways (25) succeeded in producing an epithelioma in a mouse after application of deoxycholic acid, a normal constituent of the bile. It took 776 days and occurred in only 1 of 80 mice painted. But subcutaneous injection caused the appearance of 3 spindle cell sarcomas in 5 mice which lived over 6 months. This confirmed the report of Ghiron. He found that deoxycholic acid induced fibrosarcomas in a high proportion of rats and mice injected. The tumors were transplantable. The importance of these observations cannot be overstressed, as they indicate the possibility of malignant tumor production from a compound normally present in the human body.

Numerous substitution products of these three well known carcinogenic hydrocarbons have been synthesized and tested. The importance of the position in the ring of oxygenation (26) of the methyl derivatives (30) of hydroxyl groups (3) of diazo coupling (41) etc. have been considered. These studies have been of great interest to the chemists. The London group determined that increasing the length of the carbon chain produced a rather irregular diminution of carcinogenic activity. The limit of activity seemed to be reached when seven carbon atoms were in the chain. None of these new compounds have exceeded the carcinogenic activity of methylcholanthrene.

In addition to the three carcinogens just discussed, great interest has been aroused by the production of visceral tumors in rats and mice. Kinouchi added a 3 per cent solution of dimethylaminonaphthalene (butter yellow) in olive oil to the diet of rats for 50 days. Cancers of the liver were induced. These tumors metastasized. They could be transplanted. Cancer also was brought about in the livers of mice but not in rabbits or chickens. Rats developed liver cancers in re-

sponse to subcutaneous injections of this compound. Direct application to the viscus in cholesterol pellets failed in producing carcinomas.

Some other chemicals of naphthalene and carbazole groups have been found to produce liver tumors recently (22). Nakahara et al. (101) found that liver feedings inhibited the development of liver cancers in albino rats subjected to Kinoshita's experiment with butter yellow. The same investigators (102) found also a slight inhibiting effect from yeast though the rats developed cirrhosis. However, crystalline vitamin B<sub>1</sub> failed completely as an inhibitor.

The mystery of carcinomas of the gastro-intestinal tract seemed to be on the way to solution when Roffo (121) announced that he had found such growths to follow the ingestion of fats oxidized by heat. He noted erosions, ulcers, and neoplasms of the stomach, liver, and cecum in rats fed on bread and milk to which there were daily additions of animal fats or olive oil which had been heated to 350 degrees Centigrade for ½ hour. The heat destroyed all the cholesterol according to Roffo. The fats under this treatment presented absorption spectra resembling those of the carcinogenic hydrocarbons. He believed the tumors to be due to the action of a carcinogenic oxysterol.

Widmark tested for the presence of cancer producing substances in roasted foods by painting mice every 2 days with alcoholic or petroleum ether extracts of such substances. He used horse meat heated to 275 degrees Centigrade, browned butter, and roasted coffee. No malignant tumors were recorded in male mice with extracts either of roasted or unroasted foods. Adenocarcinomas of the breast were present in 9 of 23 female mice which survived 11 months of painting with roasted foods (6 muscle, 2 coffee, 1 butter). The control series of 26 animals had only one breast carcinoma. The spontaneous tumor incidence for the strain was 10 per cent. He concluded that the extracts of roasted foods contained one or more carcinogenic agents.

Cook and Kennaway (24) were unable to confirm these experiments. They concluded that "as yet there is no convincing evidence of any specific dietary constituent in this connection." Roffo's work according to these investigators has not been supported.

In this connection, the work of Rowntree et al., who reported the production of spindle cell sarcomas in white rats fed an ether extract of crude wheat germ oil, has never been confirmed though many attempts have been made to do so. These experiments were unique at that time in that the

neoplasms had arisen when the inciting agent had entered by way of the gastro-intestinal tract.

Kagawa claimed to have noted many stomach tumors in rats fed on "butter yellow" of Kinoshita. The percentage was raised from 6 to 22 per cent when cholic acid was given simultaneously.

Tumors of the genito-urinary apparatus also have been induced by subcutaneous injections of betanaphthylamine. Papillomas, which graded from benign pedunculated types to infiltrative, sessile malignant ones were present on the base of the bladder. These tumors were first noted after 20 months in those dogs which had received fairly large subcutaneous dosages of the drug daily. Thirteen of 16 survivors showed pathological lesions (63). Degenerative changes were present also in the tubular epithelium of the kidneys and the parenchyma of the liver. There was also an anemia. Papillomas were discovered in the bladders of white rats treated with 4 oxy 2 3 dimethylazobenzol (100).

Semproni and Morelli showed that beta-anthraquinoline had weak carcinogenic action on the kidneys of white rats given subcutaneous injections of this substance. Two of 8 animals which survived 11 months had adenocarcinomas of the kidney.

It has been known that teratomas of the testis of the rooster can be produced by injection of the gonads with a 5 per cent solution of zinc chloride in the spring of the year. Falin found that he could get similar tumors of embryonic character by the injection of 10 per cent zinc sulphate. The zinc salts formed albuminates, a caustic action being their primary effect. Areas of limited focal necrosis could be identified. In the immediate vicinity, the first tumor cells could be seen. Gonocytes seemed to be stimulated by a combination of the necrotic tissues and the active spermatogenesis of the spring season. Champy and Lavedan observed that partial removal of the testis of roosters was followed by regeneration from the fragment which remained. In 15 fowls which had repeated partial castrations over a period of 3 years, 4 developed huge tumors. These were malignant seminomas and embryomas. Apparently, the repeated active regeneration sufficed eventually to initiate the neoplastic response.

Many other experiments have been made with varied materials as inciting agents for neoplastic growth. Different types of animals also have been tested. A few of the most notable of such experiments can be cited. Passey reported that dogs which had been tarred weekly from 18 months of age, developed tumors after 6¼ to 6½

years. One of these was a malignant melanoma. Spontaneous tumors have been frequent in old dogs but this report shows that a long latent period must be expected in this species.

Selbie injected thorotrast into rats and mice. Tumors occurred in 25 of 43 animals 1 year or more old. 21 of these were spindle cell sarcomas, and 3 were fibromas. In 9 mice of 60 injected, there were sarcomas. These could not be transplanted in autotransplantation and homotransplantation. Foulds used young female guinea pigs to test thorotrast. He injected 0. to 0.3 cubic centimeter undiluted into the base of the nipple 4 times. They had carcinomas and sarcomas after 38 days. These tumors were transplantable and he carried them through 15 generations. These two observations are very important since thorotrast had been used rather freely formerly as a diagnostic agent. The danger of such a radioactive metal thus has been amply proved.

Although there has been difficulty in repeating Fibiger's rat stomach nematode neoplasm results, apparently a new parasitic nematode of the East Indies may prove to have this relationship. Bonne and Sandground discovered these parasitic worms in the hypertrophied tissue masses of gastric lesions in Javanese monkeys. They considered the growths to be adenopapillomas, some of which invaded the submucosa and showed aggressive possibilities.

Takizawa produced sarcomas in mice by daily subcutaneous injections of concentrated glucose solutions for over 1 year. Galactose and fructose were also successfully used but the percentage of tumors was less. He was not successful with lactose and sucrose. Surtzoff, Babcock and Loeb (33) were able to induce sarcomas in mice by injecting them 6 times weekly with hydrochloric acid (0.25 c.c.m.) kept at hydrogen-ion concentration of 5. It took 10½ months.

The recent direction of experimental studies has been toward finding how the carcinogenic chemicals produce their effects. Experiments with tissue cultures afforded an opportunity to observe what happened to the cells directly exposed to solutions of these agents. Magat, Lebeson, and Volkson studied the effects of 1:156 dibenzanthracene on mouse and fowl tissues *in vitro*. The hydrocarbon penetrated the cells in from 2 to 18 days. No changes were noted in the rate of cell growth or in the cell metabolism. They concluded that this hydrocarbon did not provoke inflammatory growth or cell proliferation.

Earle and Voegtlin found that methylcholanthrene and dibenzanthracene even in high dilu-

tions, caused severe growth retardation and degeneration in cultures of rat and mouse fibroblasts. The damage was roughly proportional to the concentration of the reagent and to the time of exposure. In no instance was growth stimulated by either hydrocarbon.

Owen, Weiss, and Prince determined that dibenzanthracene caused stimulation of cut segments of flat worms (*Planaria*) and regeneration of the whole animal. Triphenylbenzene, on the other hand, had no effect on the segments though it stimulated reproduction of the whole animal. Glutathione gave results similar to dibenzanthracene but some amino-acids had no demonstrable action.

Hollaender, Cole and Brackett regarded the toxic effect of methylcholanthrene on yeast in cultures as a finer test for the dilution of this chemical than either the chemical or fluorescence methods.

Graffi could visualize with the fluorescence microscope the passage of carcinogenic agents into the cytoplasm of benign and malignant cells *in vitro*. He did not think that the nucleus was involved. The mitochondria seemed to have a selective affinity for these carcinogenic hydrocarbons. He suggested that the carcinogens act by deranging the cell metabolism through their effects on the mitochondria rather than by attacking the chromosomes.

Creech described an increased cell proliferation in cultures of mouse fibroblasts with some concentrations of carcinogens and a decreased cell growth with others. There was a precocious separation of the chromosomes in the prophase and metaphase with some of the carcinogens.

When paramedusa were exposed to high dilutions of 3:4 benzopyrene for long periods of time, Motttram (96) was able to identify large abnormal individuals. If these were segregated he had abnormal strains which consisted of individuals many times the normal in size, or midgets, or Siamese twin types. These aberrations could be maintained through many generations. Only a few of the exposed cells presented these changes but once they had taken place they were reproduced for many generations after the carcinogenic agent had been removed. The changes occurred among the cells long stimulated to a growth rate above the normal by exposures to the hydrocarbons.

Gey after keeping tissue cultures of rat fibroblasts exposed to these artificial conditions for years, was able to transplant them into animals. Thus the production of sarcoma *in vivo* has at length been accomplished.

The action of the carcinogens on living cells seems to be an initial retardation of growth. It can be altered by changing the concentration of the chemical and the time of application. Apparently, after long application of dilute solutions, changes may be effected in cells so that they become abnormal. Such abnormal cells breed true and can be maintained as such in the absence of the inciting agent. The change does not appear to be in the chromosomes.

The initial retardation of growth was an unexpected finding with the carcinogenic hydrocarbons in tissue cultures. It was verified quickly, however, by experiments on transplanted tumors. Haddow and Robinson (57) used several well known transplantable animal tumors and tested the influence of various carcinogenic hydrocarbons against their growth rates. Retardation was immediate, prolonged, and relatively constant. The growth of the animals themselves was retarded as well. Also their fertility was reduced.

The same growth retardation effect was found to be true for spontaneous tumor growth rates (55). Dibenzanthracene and other carcinogens usually caused a prolonged retardation of growth. Sometimes the tumors partially or completely regressed. Some supposedly noncarcinogenic hydrocarbons produced the same effect. Later, they were shown to be weakly carcinogenic. Noncarcinogenic hydrocarbons produced a transient response or none at all. The prolongation of the retardation after the cessation of injections seemed to be an effect characteristic of carcinogenic compounds. It may be attributed to a toxicity of a special and possibly a specific kind.

It was even apparent that tumors induced by a chemical carcinogen could be retarded by injection of another though these tumors were less susceptible to inhibition than either the transplanted or spontaneous tumors (56).

In an elaborate experiment 34 compounds of known carcinogenic power and 34 supposedly noncarcinogens were tested for inhibitory action on both transplanted and spontaneous animal tumors. 86.5 per cent of the carcinogenic compounds showed inhibition of growth, whereas 79.7 per cent of the noncarcinogenic compounds showed no trace of inhibition. This association of growth-inhibiting properties and carcinogenic activity appeared to be statistically highly significant. The relationship between these two qualities did not seem to be quantitative since some feeble carcinogens had marked inhibition power (58).

Lees gave single subcutaneous injections of 1,2,5,6 dibenzanthracene to young rats. He

found a prolonged inhibitory effect on their growth. It was not due to interference with their food consumption or to change in their metabolic rate. Nearly half of the animals died in 64 days. Other phenanthrenes including methylcholanthrene and 1,2 benzpyrene gave only temporary growth retardation. Jensen rat sarcoma was inhibited by 1,2,3,4 dibenzanthracene injections but the effect was less marked than that on normal tissues. Pollia could not concede a specific inhibitory effect of 1,2,5,6 dibenzanthracene on a transplantable rat sarcoma because he had inhibition from other noncarcinogenic agents. Appel et al. recorded a more rapid growth, more extensive and earlier metastases from Brown-Pearce rabbit carcinomas in animals treated with 1,2,5,6 dibenzanthracene than in the control group. The Whites pointed out that both carcinogenic and noncarcinogenic hydrocarbons retarded growth if given in the diet in adequate amounts. This varied widely with the substances used. There was a specific deficiency of the sulphur containing amino-acids in these animals. This may be related to an increased demand for organic sulphur as a detoxifying mechanism. Supplementary feedings with l-cysteine or dl-methionine caused a prompt stimulation of growth in these rats. Taurine, sodium sulphate, and glycine were ineffective. When McJunkin and Wolavka made intraperitoneal injections of an aqueous suspension of 1,2,5,6 dibenzanthracene and lecithin into rats, a transplantable rat sarcoma regressed completely in 20 of 51 animals. In many of the others the growth was slowed. Intratumoral injections were less efficacious. This tumor had resisted various other substances. Bauer reported that 7 humans with skin cancers remained healed over 2 years after the lesions had been injected with 0.5 to 1.0 cubic centimeter of a 0.5 per cent solution of 3,4 benzpyrene in ether. Twenty-two patients were treated by this method.

Some evidence has been accumulated that hemolytic activity may be one of the factors in carcinogenesis. All the strongly positive carcinogenic compounds possessed this quality on testing, while the negative compounds did not seem to have it. Confirmation of these facts has been obtained by a quantitative analysis of the iron deposited in the lymph nodes. In some experiments with carcinogenic agents there was a progressive increase in the lymph node iron to four times the initial figure (143).

Many of the carcinogenic hydrocarbons revealed a photodynamic action. There was a possibility that this might be correlated with the neoplastic

activity. But after a considerable amount of investigation this type of light sensitivity cannot be considered as of significance in connection with the carcinogenicity of the hydrocarbons.

Wolbach studied the tissue responses to carcinogens applied to the skin, subcutaneously and to the viscera. Benzo(a)pyrene in benzene was used for the epidermal painting, cholesterol pellets of dibenzanthracene for subcutaneous implantation, and "butter yellow" in the food for the liver. All three chemicals proved to be destructive agents. A constant reparative process was maintained involving repair of the damage to individual cells. Replacement of cells by division of adjacent ones also occurred. Hyperplasia was brought about by this mechanism. The injurious effects on the cells continued even during the stage of hyperplasia. These reparative responses in the regions of hyperplasia seemed to represent the stage preceding the development of true tumor. No direct chemical stimulation of cell growth was apparent.

Rondoni (13) used noncancerous substances subcutaneously. Nodules of connective tissue reaction were apparent. Regressive changes took place and there was no evidence of malignancy. Mixtures of cholesterolized liver had greater numbers of necrotizing substances so that the reaction was more intense and regressed more slowly. The sarcomatous changes from benzo(a)pyrene were first indicated by the appearance of multicentric abnormalities in the histological structure of the granulation tissue. Irregularities in the size and staining capacity of the nuclei were characteristic findings. A new race of sarcoma cells arose from the continuous action of the hydrocarbon on the labile undifferentiated cells of the reaction tissue, most likely a mutation.

Hyal conducted experiments regarding the local tissue changes following subcutaneous injection of dibenzanthracene in mice,lard being the vehicle carrying the chemical. Lard alone caused a local hyperemia for a few days, then a cavity surrounded by fibrous tissue with no degenerative changes. Lard with neosalvarsan was followed by a more intense reaction which lasted for 6 weeks and then returned to normal. A cavity was laid, lined by a syncytium and surrounded by connective tissue. Lard with the carcinogenic chemical gave changes according to the concentration. The local reaction was intense and persisted. It appeared to be irreversible if the dosage was sufficient. Degeneration and regeneration went hand in hand until finally regenerative cells began to assume more and more atypical forms in small foci. Mitoses were frequent. The cells seemed to be intermediate between macrophages and fibro-

blasts, at least they were mesenchymal with increased powers of development.

The lymphatics in acute and in chronic inflammatory lesions of mice were examined after injection with hydrokollag, a graphite preparation. Pullinger and Florey were able to demonstrate that the lymphatics were patent and unobstructed in tarred skin before and after the appearance of papillomas. The injected fluid reached and entered most of these warts. There was no sign of chronic lymphangitis. There was no overgrowth of endothelium into the lumen. Large dilated lymphatics were shown at the growing margins of 11 malignant tumors. Lymphatics were found in the center of only 1 tumor but failure to show them was not taken to be conclusive proof of their absence. The authors concluded that lymph stasis and obstruction were not essential factors in the production of benign tumors of the skin of mice.

Brunschwig, Tschetter and Biswell (14) investigated the effect of 1.5 benzo(a)pyrene on rapidly proliferating epithelium. This was done by producing an ulceration in the painted areas. In one group radium was used for this purpose and in another the actual cautery. The trauma was instituted at different time intervals from the beginning of the painting. Multiple papillomas and carcinomas occurred in all the animals. In spite of repeated applications the wounds healed and tumors did not arise in the newly formed epithelium.

Deitch excised skin from mice painted with tar or benzo(a)pyrene. Small fragments were taken from the treated areas and from distant zones. The wounds were left open and 1 day later other samples were removed. The treated areas exhibited thickening, papillomas or atypical growth according to the duration of the painting. On the other hand, the distant sites showed only those regenerative changes present in unpainted controls. No indication was given that tar or benzo(a)pyrene induced a constitutional change favorable to the development of malignant growth.

Page applied a 3 per cent solution of methylcholanthrene to the skin of 3 to 4 months old white mice, 3 times a week. There was an immediate increase in the size of the cell, nucleus, and nucleolus, the most marked change being in the nucleolus. Squamous cell carcinomas appeared within 7 weeks in this group. With benzene alone there was no change in the nucleus or nucleolus. The average nuclear and nucleolar areas in the carcinomas were greater than those in the hyperplastic epithelium of the animals in which carcinomas did not develop.

ORR (107) tested the effects of six carcinogenic hydrocarbons, ten noncarcinogenic hydrocarbons, and a group of unrelated irritants on the skin of mice. Benzene and acetone were used as the solvents, but acetone was more satisfactory as it had no effect on normal mouse skin. The carcinogens produced early epilation, with regeneration of hair, abnormal in character. Progressive thickening of the skin, loss of elasticity, and passive congestion preceded the appearance of the tumors. The significant changes before tumor growth were considered to be transformation of collagen into a fine fibered, nonrefractile type, first of the superficial but later of the whole dermis, passive congestion of the subcutis, alterations of elastic tissue in texture but not necessarily with an increase in amount, and absence of inflammatory cell infiltration. Small scars were found on the subcutis. The sites of tumors were related to these scars in a significantly high proportion. Elastic tissue hyperplasia was patchy, often with gaps at which tumors also appeared. The passive congestion probably caused an oxygen lack in the cells. The writer suggested that cancerization of epithelial cells by carcinogenic hydrocarbons was partly the result of changes in the deeper tissues. The mechanism in all probability was related to an interference with nutrition.

In a later study Orr (108) investigated the subcutaneous tissue responses. Pellets of paraffin wax containing 2 per cent carcinogenic hydrocarbons were introduced subcutaneously in mice. The animals were killed from 1 to 387 days later. With wax alone, there was a firm collagenous encapsulation within 2 months and no further change. With noncarcinogenic material in the wax, this capsule was thicker and longer in forming. When carcinogenic hydrocarbons were present, the initial reaction was the same but encapsulation was imperfect, the collagen being loose in texture and small in amount, with fibrinoid material on the inside. At a later date, cellular proliferations were found outside the collagen zone and at a distance from the pellet. The cells were of histiocytic and lymphocytic type and were the cells from which the sarcoma developed. These cells from which the carcinogen produced tumors were not present until a comparatively short time before the tumors appeared. Then, they collected outside the range of action of the carcinogen. The appearance of sarcoma in these cellular foci was apparently the result of a progressively increasing rate of division in an effort to provide an adequate fibrous capsule around the foreign body.

Brock, Druckery, and Hamperl placed benzpyrene in collodion sacs intraperitoneally. After a lapse of 8 to 12 months tumors appeared suddenly. All were sarcomas and in none could the agent be demonstrated by ultraviolet light. These growths appeared to develop at the periphery of the capsule where the concentration of benzpyrene was lowest and cell death accordingly had not taken place.

When rabbits were employed, no tumors could be made to arise at the site of direct application of 1,2,5,6-dibenzanthracene. Intravenous, subcutaneous, intramammary, intratracheal, and direct vaginal applications were made and no tumors appeared at any of the local sites within 900 days. The carcinogen had a slower action on this species but tumors were produced at sites remote from the application. Adenocarcinoma of the uterus, cholangioma and cirrhosis of the liver were noted. Burrows and Boyland (18) contrasted this peculiarity of the response of rabbits to the regularity with which tumors appeared at local sites of contact with this hydrocarbon in rats, mice, and fowls.

Efforts have been made to determine whether local acute or subacute inflammations might be effective in causing earlier localization of a carcinogen and consequent earlier tumor production. Rondoni and Corbellini (123) used a combination of painting with carcinogenic hydrocarbons and light cauterization of the area. They believed that the cauterization acted as a local realization factor. This precipitated the neoplastic development in a tissue potentially malignant from the application of the carcinogens.

Burrows, Mayneord, and Roberts (19) produced inflammatory foci in rabbits by the injection of kaolin and finely powdered silica suspended in olive oil. Each focus was given a single x-ray treatment of 600 volts. Twelve animals were started. The effective total was 9 of which 6 had tumors from 22 to 38 months following irradiation. Two tumors were of uncertain pathology but 4 were sarcomas. The probable rôle of chronic inflammation was to bring about a concentration and retention in the affected tissues of the specific agents of cancer.

Beck tested the influence of acute and subacute inflammation by combining turpentine with 3,4-benzpyrene in various ways to control the results. He made subcutaneous injections into mice. All groups injected with benzpyrene developed tumors. Fluorescence could be demonstrated in these tissues for approximately 6 months. Neither acute nor subacute inflammations had any effect on the development of sarcomas. The sarcomas



did not originate from the fibrous tissues of sub-acute inflammation.

Woglom used rats to test the effect of trauma on the localization and development of benzo(a)pyrene induced tumors. He soaked threads in a benzene solution of this chemical over night and then passed them through the viscera, kidney testis, uterus, liver, 381 animals lived from 157 to 630 days and 29 had tumors about the threads in the connective tissue. There were no tumors in any of the organs. The glandular epithelium did not have its resistance lowered by benzo(a)pyrene by this relatively gross trauma.

Mottram (97) painted mice with benzo(a)pyrene in benzene for 75 days. Then 1000 r gamma Ir radiation was followed by a greater number of epithelial tumors than in the controls. If doses destructive to the epithelium were used as Cramer did (14,000 r to 18,000 r  $\beta$ -rays) the epithelial tumors were inhibited under the same conditions.

Mottram (98) continued this research by painting mice with benzo(a)pyrene long enough to produce warts. Then, a single dose of  $\beta$ -radiation was given. Benign and malignant tumors both appeared. All the tumors were in areas receiving from 800 to 2800 r. None occurred in areas receiving less than 800 r and none arose under the radium applicator when the dose was 6000 r.

Kidd and Rous injected papilloma virus (Shope) into the blood stream of rabbits whose ears had been tarred 1½ to 3 months previously. This stimulated the growth of the tar warts with the production of squamous cell carcinoma.

Brunschwig (15) painted rabbits ears with benzo(a)pyrene 3 times a week for 120 to 375 days. One out of 40 developed a carcinoma at the two hundred and twentieth day. In a smaller group of 19 animals treated similarly but injected with extracts of human warts, developed cancer. He concluded that on occasion the human wart virus might hasten the malignant degeneration of benzo(a)pyrene warts.

The possibility that the process of carcinogenesis might be related to some chemical reaction involving the carcinogen has been a stimulus to investigators. The general effects have been more difficult to unravel as the chemistry is involved and perhaps the agents were present only in minute traces. Sobotta and Bloch made lipid extracts of 2100 liters of pooled urine from cancer patients. There was no positive chemical or biological evidence for the presence of carcinogenic hydrocarbons. They were able to detect small quantities of dibenzanthracene and phenanthrene added to 100 liters of normal urine so that the method seemed adequate.

There must be attempts of the tissues to eliminate these agents. Some evidence has been obtained by Dobriner, Rhoads, and Lavin following injection of 1:2 5:6 dibenzanthracene into rabbits, rats, and mice. The urine and feces were examined for any derivatives and the phenolic fraction of the excreta from rabbits gave an absorption band not present in normal animals. It was also not that of dibenzanthracene. A crystalline substance was obtained from this fraction. It proved to be noncarcinogenic for mice.

Chalmers injected mice intravenously with colloidal solutions of 3:4 benzo(a)pyrene, methylcholanthrene and cholanthrene. The fluorescence spectra of the bile, urine, and feces were examined. After benzo(a)pyrene was injected, the bile showed a spectrum different from that of benzo(a)pyrene due to some substance (named B P X) insoluble in ether. There was a substance also in the feces probably identical with B P X. A second substance in the feces was ether soluble and had a spectrum differing from B P X. The urine gave a general fluorescence not banded. The same was found to be true for all the excreta following the injections of methylcholanthrene and anthracene.

After intraperitoneal injections in lard or colloidal watery solutions of 1:2 5:6 dibenzanthracene into mice, only 40 per cent could be demonstrated by fluorescence 23 days later. Within 3 weeks almost all the lard injected material had vanished and only 1/5 of the colloidal material remained. The delicacy of this test made it apparent that the mouse was able to metabolize this carcinogen. The hydrocarbon suffered rapid alteration in the animal body. Some chemical reaction occurred which exhausted most of the carcinogen before tumors began to appear (41).

Hieger could not detect by fluorescence spectroscopy the carcinogenic hydrocarbons in extracts of mouse and rat skin 4 weeks after their last application.

Reggiani, Danai, and Morelli after intravenous injection of 3:4 benzo(a)pyrene in rats found that extracts of the liver gave an absorption spectrum different from that of benzo(a)pyrene.

Intravenously injected benzo(a)pyrene in mice was retained by the body fats, and excreted as an altered substance in the bile. The colloidal benzo(a)pyrene could be found in the blood serum, the central nervous system, and the sebaceous glands. Some pregnant mice had this hydrocarbon in the placenta but it could not be found in the fetus. Traces were found in the milk from lactating breasts of mice (Chalmers).

Other changes of a general nature have been observed by Lewis. Certain tumor bearing animals had a severe neutrophilia in the peripheral blood and a myeloid hyperplasia of the spleen, bone marrow, and lymph nodes. In them, areas of myeloid infiltration were found in the adrenals.

Similar systemic effects were noted by Parsons. The picture of the lymph nodes was similar to that from lethal or sublethal doses of x-rays. Twort and Twort observed a correlation between hyaline degeneration and enlargement of the spleen and the carcinogenicity of the agent applied.

Congo-red has been removed from the circulating blood of normal rabbits at a definite rate. After painting the animals with carcinogenic hydrocarbons for a year this normal removal rate tended to disappear (Hoch-Ligeti).

Roffo (120) claimed that when cancer of the skin was induced in white rats by the influence of sunlight, it was due to a concentration of cholesterol in the skin. This compound was then rendered photosensitive by the ultraviolet irradiation it received.

Mayneord and Roe found that cholesterol, previously irradiated with ultraviolet light, x-rays,  $\beta$ - or  $\gamma$ -rays from radium produced an appreciable blackening of the photographic plate in the vicinity. The effect also could be obtained by prolonged heating. It could not be brought about *in vacuo*. They believed that probably an unstable ozonide or peroxide was formed. No evidence of an absorption spectrum resembling any of the carcinogenic hydrocarbons could be found although 40 specimens irradiated under different conditions were examined.

Bergmann et al. studied the effects of the application of irradiated cholesterol to the skin of mice. Neither benign nor malignant tumors were produced though the treatment was extended over a period of  $2\frac{1}{2}$  years.

Schmid injected 0.2 per cent irradiated ergosterol in linseed oil into the gall bladder of guinea pigs. The cystic ducts were ligated. The animals were sacrificed in from  $3\frac{1}{2}$  to 9 months and though the glandular elements had penetrated into the submucosal tissues, no true tumors were found. Perhaps the elapsed time was not sufficient.

Buengeler experimented upon three groups of mice with photosensitive substances. Eosin, hematoporphyrin, and tar in dilute solutions were injected subcutaneously twice weekly. The animals were exposed to sunlight daily for 4 to 5 hours over a period of 210 days. There was a high mortality. The reaction could be divided into three types. In the early weeks acute in-

flammation was manifested by conjunctivitis, dermatitis, eczematous skin reactions, vesiculation, and ulceration. In a later period after 2 months there was a progressive loss of hair, atrophy of the epidermis, mast cell infiltration, and a hypertrophy of the connective tissue. From 3 months on tumor formation was apparent. It was a gradual imperceptible change from the proliferative process. At first the tumors were benign—papillomas and fibromas. But after 6 months many of the tumors became malignant. The tumors were multiple usually. Squamous cell carcinomas and spindle cell sarcomas were the commonest forms of malignancy. Myeloid leukemia and tumors in the lung were also noted. Degenerative changes were present in the organs, as well as amyloidosis, and hemorrhagic necroses of the gastric walls.

Taussig et al. tried the effect of light on benzpyrene painted mice. They found no significant differences between the tumor incidence in the dark, light sensitized, and light kept mice.

Rusch and Baumann irradiated mice daily with a mercury quartz light. Papillomas, epitheliomas, and spindle cell sarcomas were developed on the ears in from 35 to 82 per cent. These tumors could be transplanted. Their incidence was lower in black mice. Irradiation for long periods was productive of more tumors than short period irradiation. A high fat diet produced tumors most rapidly, cholesterol had no effect when added to the diet. Brain and liver in the food caused retardation in tumor production. In the rat, Roffo's observation of increase in the cholesterol content of the skin by ultraviolet irradiation was confirmed. But in the mouse and guinea pig there was no increase under these circumstances.

Doniach and Mottram (35) showed that the skin of white mice painted with carcinogenic hydrocarbons became sensitive to blue violet rays of the visible spectrum. They demonstrated that the skin under these conditions became red and edematous.

Morton, Luce-Clausen, and Mahoney (94) found that white mice of the Swiss albino Bar Harbor strain kept in the dark and painted with 0.5 per cent 3.4 benzpyrene in benzene twice weekly for 17 weeks developed a much higher percentage of carcinomas over the next 2 months than a similar group kept in visible light. Ultraviolet light was excluded. These results indicated that the carcinogenic agent 3.4 benzpyrene could induce skin tumors in mice in total darkness. Ordinary light apparently had a retarding action on the carcinogenic process.

Doniach and Mottram (36) confirmed these observations. They pointed out that though tar and benzo(a)pyrene produced a greater dermatitis in the light, light is not essential for tumor production. They painted mice with benzo(a)pyrene and cholanthrene, purified in the dark. Tumors were produced in the skin of mice by both agents though the mice were kept in total darkness. The effect of darkness was to reduce the dermatitis to a minimum. There was no inhibition of tumor production or hair growth. The effect of strong sunlight upon the similar chemically painted skins of mice was to increase dermatitis and to reduce tumor production. Perhaps this action was due to the photodynamic properties of the hydrocarbons. The cells which took up the chemicals were sensitized to light and many of them have been seriously damaged or killed.

These observations fit with the biological effects of light upon plant life. It is known that light exerts an inhibiting effect on the growth of plants. The growth is much more rapid in the dark. It is at its maximum rate just before sunrise. Sprouting is therefore carried out in the dark by many agriculturists. The heliotropism of growing plants is partly due to the greater growth rate of the stem away from the light.

Lacaze's demonstration that estrogens had carcinogenic properties inciting mammary cancers in mice led to much activity in this line of investigation. The work was confirmed and extended in many laboratories. The hormones had an appeal to the investigator as they were normally occurring growth stimulators and not chemical substances unlikely to be encountered in the animals. They were shown to have specific effects on the genital tissues. They became available in purified, concentrated forms.

Methods of administration have been worked out. Subcutaneous injection has been used most commonly. The estrogens have been dissolved in various solvents such as benzene, oils, chloroform, alcohol. Pellets of the substances have been implanted for long, slow action. Local applications to epithelium or injections into organs or tissues have been employed. The substances have been given orally but although not impaired by digestion, the method has been less effective. Intraperitoneal injections have been carried out.

Estrogens have been demonstrated in many tissues in the human—the ovaries, placenta, blood, urine, bile, feces, etc. The hormones may be rapidly destroyed, probably by the liver in an oxidation process. After oral or hypodermic administration, about 30 per cent has been excreted in the urine or feces. The estrogens disappeared

rapidly after intravenous administration. The urine of humans of both sexes and at all ages has been shown to contain female sex hormones, possibly indicating extragonadal sources of these secretions.

Some of the first work has been to define the normal physiological actions of the estrogenic substances. The studies of sex differentiation and the internal secretions has resulted in a brilliant advance in our knowledge of these complex relationships.

Only a few of the many excellent endocrine investigations in relation to cancer can be reviewed briefly here. It was demonstrated that male mice of high breast tumor strains could be made to develop mammary cancers by long continued injections of estrogens. Males from very low breast tumor strains could not be influenced in this way but females of the strains have been made to develop tumors after very prolonged estrogenic stimulation (1).

A 6 years summary of the effects of weekly injections of estrogenic hormones on 6 pure strains of mice showed that mammary cancers occurred only in those strains in which they developed spontaneously. They were present in larger numbers and at an earlier age in the males as well as the females in the susceptible strains. Sarcomas were noted at the injection sites and often around the oily cysts in some of the mice. No spontaneous sarcomas were seen in these strains (Lacaze, 68).

Sarcomas developed in 10 of 227 mice injected with ovarian hormones over long periods of time according to Burns et al. The growth seemed to start suddenly in contradistinction to the step by step gradual change when carcinomas arose.

Nelson reported that, when guinea pigs were given estrone in oil for 2 to 3 months subcutaneously fibromyomas of the uterus and adenomatous hyperplasia of the endometrium were observed. In the cervix there was metaplastic downgrowth and pearl formation.

Loeb et al. (79) were unable to find any precancerous or cancerous changes in the uterus of 300 mice injected with estrogens though some showed penetration of the uterine glands into the muscle and metaplasia of the epithelium.

Gardner et al. (46) reported 'the first convincing demonstration of a malignant cervical tumor induced by estrogen in mice. The previously observed epithelial hyperplasias of the cervix were probably also precancerous. This tumor was grafted successfully into male and female mice of the same strain. The tumor grew rapidly without further estrogen stimulation.

Loeb et al (80) believed that estrogens affected the stroma of organs in two opposite directions. By inducing growth processes of the epithelial structures the amount of hyaline fibrous material in certain organs—vagina, cervix, uterus—may be diminished. Or, if large doses were administered over long periods, the opposite was obtained—marked increase in fibrous and hyaline material in the stroma similar to the changes of old age. Suntzeff et al (134) showed that this hyalinization of the uterus was reversible when the estrogen injections were stopped. The mammary glands continued on to cancer indicating that here the stimulus could become manifest many months after the estrogen had ceased to act.

When 4 pure lines of mice had been receiving estrogenic hormones, a considerable number of lymphosarcomas were noted. Eleven of these originated in the thymus. No mice of these strains had such tumors spontaneously in 5 years of observation (Lacassagne, 69). This has been confirmed by Gardner (47).

Robson and Bonser induced mammary cancer in male mice of a susceptible strain by weekly injections of a synthetic estrogen, triphenylethylene. Lacassagne (70) did the same thing with another synthetic estrogen, diethyl stilboesterol. Geschickter used the latter agent which is not a sterol. He induced cancer of the breast in 1 rat. Mammary cancers were obtained in 26 others with estrone. This strain never had spontaneous cancer of the breast.

Gardner, Strong, and Smith (50) found that the mammary glands in mature female mice of strains of high susceptibility to spontaneous tumor development had more localized nodules than those of the low tumor strains. These nodules were made of hyperplastic, resting, or regressing glandular tissue. If normal factors were responsible for them, there must be additional local factors to account for their localization.

Van Gulik and Korteweg could not determine a great difference in the estrous cycles of high and low strain tumor mice. But there was a difference in susceptibility to follicular hormones, some strains requiring more to affect them than others. The genital organs of the two high breast cancer strains were less susceptible to follicular hormone than those of the three low breast cancer strains. Under normal conditions the females whose genital organs were least affected produced the greatest quantity of follicular hormone.

Wolfe (150) studied rats for a comparison of estrous cycles, fertility, and tumor incidence. The strain with low fertility was associated with a high tumor incidence.

The possibility that overtreatment with estrogenic substances was responsible for a cancer of the breast in the human was suggested by Auchincloss and Haagensen.

The mammary glands of the monkey have proved resistant to estrogenic stimulation. The Yale group has worked for 5 years on this species with negative results to date.

The pituitary gland has been caused to undergo changes following long continued estrin injections. Marked enlargement of the anterior part may be seen especially in rats. There may be intense congestion. The entire gland may be almost entirely chromophobe cells with practically complete absence of acidophils. Definite adenomas in the rat have been produced by Wolfe and Wright (152) and Zondek among others. The latter investigator noted a retarded growth and inhibited sexual development as well. The pituitary tumors had the same amount of gonadotropic hormone as the normal pituitary animals. This suggested that it was not the production of the hormone but its utilization that was inhibited. Lacassagne (73) could not see a correlation between the hypophyseal changes and cancer susceptibility in 4 strains of mice treated with estrogens. The pituitaries varied from no change to adenomas, sometimes malignant. Perry (114) had pituitary tumors in 3 of 131 mice receiving estrone treatment.

Turner and Gomez (138) were convinced from their experiments that production of mammary tumors in male mice of susceptible strains by the long continued application of ovarian estrogens was effected by way of the pituitary—a mam-mogen being responsible.

Loeb and Kirtz (78) transplanted anterior lobes of hypophyses into inbred strains of mice. This caused marked development and secretory activity in the mammary glands of these strains. An increase in the cancer rate in virgin mice was noted as compared to that in similar virgin mice without the hypophyseal transplants. Cancer could not be induced by this means in the low cancer strains. Presumably the effect was from increased production of estrogen in the ovaries because of these transplants.

Lacassagne (72) could not cause development of the mammary glands in male mice which had been hypophysectomized though he injected them with estrogenic substance for 152 days. Male mice of a high breast cancer strain R 111 were injected weekly with estrone benzoate. When a marked degree of hyperplasia of the breasts had been established, hypophysectomy was carried out 2 or 3 months later. In spite of

continued treatment with the estrogen, the breasts rapidly atrophied. When carcinoma of the breast had been induced by estrone, hypophysectomy caused only temporary regression with resumption of the growth.

The adrenal gland has reacted to estrogen treatment as well. Cramer and Horning (29) painted mice for 5 to 6 weeks with estrin. Both series showed a brown degeneration of the zona reticularis into the medulla. This was found in spontaneous high mammary cancer mice also. It was always fully developed before cancer appeared.

Dobrovolskaya Zavadskayas and Pessini (34) did not regard this association of brown degeneration and cancer formation as significant, but thought it related to an endocrine disturbance. They had mice with it, without cancer and vice versa.

Cramer (28) believed that in spontaneous cancer the adrenal medulla was affected, whereas in induced estrogenic cancer the zona reticularis outside the medulla was involved.

Woolley, Fekete, and Little ovariectomized mice at birth. In these animals the adrenal cortex took over the hormonal functions of the ovary enough to bring about a normal development of the uterus and mammary glands. In high mammary cancer strains it could even lead to carcinogenesis in the mamma.

Gardner and Pfeiffer (49) showed that while bone was being resorbed from the pubic region in mice under estrogen treatment, it was being deposited in some of the long bones, almost obliterating their marrow cavities.

Lacouragne and Raynaud (74) infected mice of R III strain with testosterone twice weekly from 1 to 30 days after birth until death of the mice. The mortality was high. None of the mice which lived developed mammary carcinoma. The normal incidence of this strain has been 60 to 70 per cent in the females. The mammary glands did not develop which may have been the reason for the absence of mammary cancer.

Wolfe and Hamilton (5) inhibited or reduced the incidence of mammary tumors by a simultaneous injection of androgens with optimal doses of estrogens for tumor production. Flaks and Ber inhibited the induction of methylcholanthrene cancers by large doses of testosterone. It was necessary to apply minimum doses of the chemical and maximum doses of the hormone to get this effect. Malsin et al. could not increase the incidence of tumor in mice receiving applications of benzyrene to the skin and simultaneous injections of testosterone. No tumors developed at the site of injections.

In male breast hypertrophy Hoffman has had some successful regression following testosterone therapy. Anterior pituitary hormone therapy was without effect.

Pybus and Miller noted that spontaneous bone tumors in their mice occurred  $3\frac{1}{2}$  times as frequently in males as in females. They also were present  $\frac{1}{2}$  months earlier.

Marine and Rosen presented evidence that lymphomatosis in their fowls was closely associated with a deficiency of male hormones. This was manifested by absence of comb growth in all 16 and absence of testicular tissue in 11. In the remainder, there were atrophic fragments of testis. All birds which developed the disease were typical capons.

The androgens can be administered to humans by mouth without clinical benefit although a much smaller dose intramuscularly will be effective. The hormone was not passed out in the feces, but absorbed from the intestine into the blood stream and eliminated by the kidneys (Dorfman and Hamilton).

The melanin pigment formation in the human skin may be related to the androgens and to the hormones of the adrenal cortex.

Larionow was unable to demonstrate any morphological alterations in the ovary, testis, thyroid, thymus, parathyroid, suprarenal, hypophysis, or pancreas in mice painted with benzyrene. He concluded that it was not by way of the endocrine system that the action of carcinogenic compounds was effected. This did not exclude their participation in the process of origin in spontaneous tumors.

Von Haam and Cappel studied the various hormonal effects on fibroblasts *in vitro*. Estrin was a slight growth stimulator, progesterin had a remarkably inhibiting effect, testosterone was inhibiting, thyroxine was moderately stimulating in proper concentration. Insulin caused an unmistakable increase in growth—as much as 10 times the normal with rapid accumulation of fat droplets and transformation of the tissues at the margin into fat cells. Adrenalin deteriorated rapidly. It was an inhibitor. Cortin was also a pronounced inhibitor.

Nadimatsu inhibited Kato rabbit sarcoma growth by large doses of posterior pituitary lobe hormone. Anterior gonadotropic hormone gave a similar result, growth hormone from anterior lobe accelerated tumor growth. Complete or incomplete extirpation inhibited the growth, as also did irradiation of the pituitary by x-rays.

Moppett thought that implanted tumors were stimulated by extracts of the anterior lobe con-

taining both growth and gonadotropic hormones Thyroxin on the other hand retarded the growth

Bischoff and Long were unable to influence the onset or incidence of adenocarcinoma of the breast in Marsh-Buffalo mice by the injection of prolactin. The ovaries underwent an enormous hyperplasia and presumably a marked hyper-ovarian function resulted

Druckery produced no effect on transplanted tumors by prolactin injections. Earlier work showed castration to have inhibitory effects on transplanted tumors

Ball and Samuels found that the growth of Walker rat tumor 256 was much slower in hypophysectomized male rats than in those controls fed an equal amount by stomach tube. Control tumors were 3.3 times as large at end of 3 weeks. The change in tumor growth was abrupt, indicating a direct effect of the removal of pituitary secretion. Adrenal cortical extract had no effect. Atrophy of adrenal cortex cannot be held responsible

Ovarian castration inhibited the appearance and evolution of tar induced tumors in rabbits (Tavares and Morais)

Benzpyrene was estrogenic for mice in doses between 4 milligrams and 31 milligrams (Perry, 113). Sarcoma produced by benzpyrene stopped the estrous cycle when grafted subcutaneously in rats but the cycle was resumed upon the removal of the grafts (Halberstaedter and Back)

From these studies it may be gathered that the hormones have a definite part in carcinogenesis. The interaction of the various glands of internal secretion serve to confuse the parts played by each one. The genetic factors must also be taken into consideration. These seem to vary from strain to strain and there can be no doubt that some factors are extrachromosomal in inheritance

The demonstration of a breast factor by Bittner may be an explanation of part of the difficulty. He showed that first generation mice from high breast cancer strains when foster fed by mothers of low cancer strain had a low cancer incidence. When the opposite experiment was done, the reverse was true. Something was passed to the sucklings from the mother's milk which modified their future tumor incidence. This means that in the development of mammary cancer in mice, the investigator must take into account the genetic factor, the extrachromosomal factor, the foster nursing factor, perhaps the functional activity factor as well as the hormonal one. This latter in itself, may be the result of an interplay between several hormones. The reason for localization of cancer in one breast must depend on

some local peculiarity. The anatomical development of the breast is regulated by the pituitary and the ovarian hormones. When the breasts have been developed to certain stages step by step through cyclic proliferations and regressions, after a sufficient latent period, the genetic behavior of these organs can be demonstrated (Lacassagne, 71). The intrinsic factors may be overwhelmed by the administration of estrogens over long periods no matter what the normal reaction would have been. This overthrow of inherited resistance is similar to that produced by any other inciting agent such as x-rays. The evidence at present seems to be against an antagonistic action of male hormones or at least their action is feeble. Similarly, progesterone has little if any effect on the development or stimulation of mammary tumors. Whether there are other factors so that there is a synergistic action between adrenal cortical hormone and estrin with thyrotropic pituitary hormone as antagonist to these two, with perhaps adrenal medulla as another antagonist (Cramer, 28) must remain for future investigation. At any rate it remains true that, "we are completely ignorant as to the mechanism whereby estrone produces cancer of the breast in the mouse" (Dodds as quoted by Gardner, 48, in his excellent review of this subject).

Whereas estrin acts mainly on the breasts, it has been shown to have effects on the cervix for cancer induction as well. Sarcomas have arisen at the injection sites. And lymphoid malignancies have been noted. Cystic endometrial hyperplasias, metaplastic changes in the uterus and pyometra have been frequently observed. Hypertrophy and myxomatous transformation of the connective tissues of the cervix and vagina have been noted. Bone resorption of the pubis and overproduction of bone in the long bone shafts have taken place. Adenomas of the pituitary gland were seen by many observers. Thus, the action of this hormone is more widespread than it was formerly thought, when it was supposed to be confined to those tissues for which it was a normal stimulant.

The other hormones, in a like manner, are being more extensively studied. Better preparations are available. There can be no doubt that their place in carcinogenesis will be clarified in the next few years.

Before hastening into print with remarkable new discoveries, it would be well for some investigators to study the historical development of cancer research. In the early years, it was known to all cancer workers that animals which were sick or undernourished were unsuitable for cancer

experiments. Only the very healthy animals were used because the others would not grow cancers. A few tumors which were demonstrated after manipulation with potent chemicals were not considered significant especially if the normal cancer incidence of the animals was not known. It has become increasingly evident that some of the highly susceptible mouse tumor strains have latent tumor possibilities which can be lighted up by almost any inciting agent. In such cases, one must be exceedingly cautious in his conclusions.

#### CONCLUSIONS

The number of known chemical carcinogenic agents is large. There is no evidence that a definite chemical structure is necessary for carcinogenic activity. These chemicals vary from simple acids and alkalis (HCL, NaOH) metal salts ( $ZnCl_2$ ,  $ZnSO_4$ ) radio-active compounds (thorotrast) sugars (glucose) to complicated dyes (dimethylaminobenzene) hydrocarbons (3,4 benzyrene, 1,2:5,6 dibenzanthracene, methylcholanthrene) estrogens (complicated sterols) and viruses (heavy proteins).

Methods for testing the carcinogenic action of the chemicals have been evolved by careful laboratory investigations.

The "average time" required for tumor production is that which is required to produce tumors in about one-half of the animals tested.

The effective total is that number of animals which is still living when the first tumor appears and is observed.

The "maximum effective" or "limiting dosage" is important as an indication of the quantity of the carcinogenic agent to which the tissues can show a response. The limiting dosage varies from species to species.

There is an intrinsic factor for cancer susceptibility or resistance handed down in inheritance. This factor may not necessarily be genetic, but extrachromosomal at times as well. Pure strain animals make possible better controlled observations.

Sex and season should be taken into consideration. Also the vehicle-solvent may not be disregarded.

The known life histories and spontaneous tumor incidence are important.

The carcinogens may unmask the latent spontaneous potentialities of the strain. Certain chemical carcinogens seem to have selective action on certain tissues.

Epithelial growths, sarcomas, and visceral carcinomas can now be induced by chemical means.

Different species have tendencies toward different types of tumors. Each species has its own characteristic tumor rate, organ susceptibility and latent period. It varies with the strain.

The carcinogenic chemicals have a toxic action. Locally they damage the tissues so that the reaction to them is imperfectly developed. Their initial effect is one of growth inhibition. The damaged tissues may release substances which modify the neighboring cells much as Spemann's evocators do. The cancerization appears to originate in the region but not directly at the site of application of the carcinogen. All the strongly positive carcinogenic chemicals cause some hemolysis. Most of the powerful carcinogens have a photodynamic action. But light is not essential for tumor production. The chemical carcinogens undergo metabolic changes in the body.

In attempting to detoxify these chemical agents, the essential sulphur containing amino-acids may be used up. Some of the carcinogens are changed in the liver and intestine giving different fluorescence spectra than the originals. They are eliminated as sulfonated and phenolic compounds in some cases. There are general systemic effects following their application noted in the blood, lymphoid apparatus, vascular system, and kidneys.

This process may be considered as one of physiological aging. In young animals the carcinogens precipitate the changes toward senility. Tumor age is shortened (Murray Milder and Morton, 95).

The hormones are naturally occurring potential carcinogens. Under ordinary circumstances their functions are physiological regulation. In repeated forced action they may become potent carcinogens. The estrogens may be rapidly destroyed by oxidation in the liver. They are excreted in the urine and feces.

Many hormones are synergistic with or as antagonistic to other hormones. They can be studied by accentuation of their normal action or by complete removal of the organ responsible for them. Under such circumstances overdevelopment of certain organs may occur or atrophy.

Cancers may be induced in the overdeveloped organs or prevented by not having an organ to function.

The process of cancerization still remains a mystery in its final steps.

#### BIBLIOGRAPHY

1. APPEL, M., STRAUS, A. A., KOLCHER, G. and NEUBERGER, H. The effect of 3,5,6 dibenzanthracene on the growth of Brown-Pearce rabbit carcinomas. *Am. J. Cancer*, 93, 23 230-245.

- 2 AUCHINCLOSS, H., and HAAGENSEN, C. D. Cancer of the breast possibly by estrogenic substance. *J Am M. Ass.*, 1940, 114 1517-1523.
- 3 BALL, H. A., and SAMUELS, L. T. Relation of the hypophysis to the growth of malignant tumors. IV. A study of the influence of nutritional factors on Walker tumor 256 in relation to the effect of hypophysectomy. *Am. J. Cancer*, 1938, 32 50-56.
- 4 BAUER, K. H. Fortschritte der experimentellen Krebsforschung. *Arch f klin Chir.*, 1937, 189 123-184.
- 5 BAUMANN, C. A., and RUSCH, H. P. Effect of diet on tumors induced by ultraviolet light. *Am J Cancer*, 1939, 35 213-221.
- 6 BECK, S. On the failure of acute and subacute inflammation to influence carcinogenesis with 3,4-benzpyrene. *Brit J Exp Path.*, 1938, 19 319-323.
- 7 BERGMANN, W., STAVELY, H. E., STRONG, L. C., and SMITH, G. M. Studies on the hypothetical carcinogenicity of irradiated sterols. *Am. J. Cancer*, 1940, 38 81-85.
- 8 BISCHOFF, F., and LONG, M. L. Endocrine factors influencing tumor development. Effect of prolactin upon the Marsh-Buffalo adenocarcinoma. *Endocrinology*, 1938, 23 327-329.
- 10 BONNE, C., and SANDGROUND, J. H. On the production of tumors bordering on malignancy in Japanese monkeys through the agency of *Noctua noctui*, a parasitic nematode. *Am J Cancer*, 1939, 37 173-185.
- 11 BONSER, G. M., STRICKLAND, L. H., and CONNALL, K. I. The carcinogenic action of oestrone, induction of mammary carcinoma in female mice of a strain refractory to the spontaneous development of mammary tumors. *J Path. & Bacteriol.*, 1937, 45 709-714.
- 12 BROCK, N., DRUCKER, H., and HAMPERL, H. Zur Wirkungsweise cancerogener Stoffe. *Arch. f klin Chir.*, 1939, 194 250-263.
- 13 BRUNSCHWIG, A., and BISSELL, A. D. Production of osteosarcoma in a mouse by the intramedullary injection of 1,2-benzpyrene. *Arch Surg*, 1938, 36 53-60.
- 14 BRUNSCHWIG, A., TSCHETTTER, D., and BISSELL, A. D. Wound healing and neoplasia. An experimental investigation. *Ann Surg*, 1937, 106 1084-1088.
- 15 BRUNSCHWIG, A., TSCHETTTER, D., and HAMANN, A. Observations on the injection of human wart (*verruca vulgaris*) extracts into rabbits with benzpyrene papillomas on the ear. *Am J Cancer*, 1940, 38 50-54.
- 16 BUENCLER, W. Ueber den Einfluss photosensibilisierender Substanzen auf die Entstehung von Hautgeschwuelsten. *Ztschr f Krebsforsch*, 1937, 46 130-167.
- 17 BURNS, E. L., SUNTZEFF, V., and LOEB, L. The development of sarcoma in mice injected with hormones or hormone like substances. *Am. J. Cancer*, 1938, 32 534-544.
- 18 BURROWS, H., and BOYLAND, E. Neoplasia in rabbits following the administration of 1,2,5,6-dibenzanthracene. *Am J Cancer*, 1938, 32 367-382.
- 19 BURROWS, H., MAYNEORD, W. V., and ROBERTS, J. L. Neoplasia following the application of x-rays to inflammatory lesions. *Proc. Roy Soc. London, Ser B*, 1937, 123 213-217.
- 20 CHAMBERS, J. G. Elimination of 3,4-benzpyrene and other polycyclic hydrocarbons from the mouse. *Bio Chem J*, 1948, 37 271-278.
- 21 CHAMPY, C., and LAVEDAN, J. Production des tumeurs par régénération entretenue dans les testicules des oiseaux. *Compt rend acad d sc.*, 1938, 207 99-100.
- 22 COOK, J. W. Cancer producing chemical compounds. *Nature*, 1940, 145 335-338.
- 23 COOK, J. W., and KENNAWAY, E. L. Chemical compounds as carcinogenic agents. *Am J Cancer*, 1938, 33 50-97.
- 24 Idem. *Am J Cancer*, 1940, 39 381-428.
- 25 COOK, J. W., KENNAWAY, E. L., and KENNAWAY, N. M. Production of tumors in mice by deoxycholeic acid. *Nature*, 1940, 145 627.
- 26 COOK, J. W., MARTIN, R., and ROE, E. M. F. Photo-oxides of carcinogenic hydrocarbons. *Nature*, 1939, 143 1020.
- 27 COTTINI, G. B., and MAZZONE, G. B. Effects of 3,4-benzpyrene on human skin. *Am J Cancer*, 1939, 37 186-195.
- 28 CRAMER, W. The hormonal etiology of breast cancer. *Am J Cancer*, 1940, 38 463-472.
- 29 CRAMER, W., and HORNING, E. S. Adrenal changes associated with oestrin administration and mammary cancer. *J Path. & Bacteriol.*, 1937, 44 633-642.
- 30 CREECH, E. M. H. Carcinogenic and related non-carcinogenic hydrocarbons in tissue culture. *Am J Cancer*, 1940, 39 149-160.
- 31 DIETRICH, D. Die Regeneration der mause baut bei Vorbehandlung mit cancerogenen Stoffen. *Ztschr f Krebsforsch*, 1938, 48 187-203.
- 32 DOBRENER, K., RHODAS, C. P., and LAVIN, G. I. Conversion of 1,2,5,6-dibenzanthracene by rabbits, rats and mice. Significance in carcinogenesis of this conversion. *Proc. Soc. Exper Biol & Med*, 1939, 41 67-69.
- 33 DOBROVOLSKAIA-ZAVADSKAIA, N. Les doses minimales de 1,2,5,6-dibenzanthracène capables de produire en une seule injection sous-cutanée un cancer chez la souris. *Compt. rend Soc. de biol.*, 1938, 129 1055-1057.
- 34 DOBROVOLSKAIA-ZAVADSKAIA, N., and PEZZINI, Z. M. Dégénérescence des capsules surrénales chez les souris de différentes lignées cancéreuses. *Compt rend Soc. de biol.*, 1939, 131 240-243.
- 35 DONIACH, I., and MOTTRAM, J. C. Sensitization of skin of mice to light by carcinogenic agents. *Nature*, 1937, 140 588.
- 36 Idem. On the effect of light upon the incidence of tumors in painted mice. *Am J Cancer*, 1940, 39 234-240.
- 37 DORFMAN, R. I., and HAMILTON, J. B. Urinary excretion of androgenic substances after intramuscular and oral administration of testosterone propionate to humans. *J Clin Invest.*, 1939, 18 67-71.
- 38 DRUCKER, H. Hypophysenverdrücker und Krebs. *Ztschr f Krebsforsch*, 1937, 45 352-354.
- 39 FARLE, W. R., and VOEGTLIN, C. Mode of action of methylcholanthrene on cultures of normal tissues. *Am. J. Cancer*, 1938, 34 373-390.
- 40 FALIN, L. I. Experimental teratoma testis in the fowl. *Am J Cancer*, 1940, 38 109-211.
- 41 FIESELE, L. Carcinogenic activity, carcinogenic structure, and chemical reactivity of polynuclear aromatic hydrocarbons. *Am J Cancer*, 1938, 34 37-124.
- 42 FIESER, L., and NEWMAN, M. S. Methylcholanthrene from cholic acid. *J Am Chem Soc*, 1935, 57 921.



43. FLAHER, J. and BIER, A. Action inhibitrice de l'hormone mâle sur la formation des cancers, produits par les substances cancérogènes. *Bull. de l'Ass. franc. p. l'étude du cancer*, 1939, 38, 68-76.
44. FOOTLE, L. Production of transplantable carcinoma and sarcoma in guinea pigs by injection of thiostratin. *Am. J. Cancer*, 1936, 35, 365-373.
45. GARDNER, W. U. Personal communication.
46. GARDNER, W. U., ALLAN, E., SMITH, G. M. and STROSS, L. C. Carcinoma of the cervix of mice receiving oestrogens. *J. Am. M. Ass.*, 1938, 11, 87-88.
47. GARDNER, W. U., KIRSCHBAUM, A., and STROSS, L. C. Observations on lymphoid tumours in mice receiving oestrogens. *Arch. Path.*, 1940, 39, 7.
48. GARDNER, W. U. Estrogens in carcinogenesis. *Arch. Path.*, 1939, 37, 53-70.
49. GARDNER, W. U. and PRIESTER, C. A. Skeletal changes in mice receiving oestrogens. *Proc. Soc. Exper. Biol. & Med.*, 1935, 37, 678-679.
50. GARDNER, W. U., STROSS, L. C. and SMITH, G. M. The mammary glands of mature mice of strains which vary in susceptibility to spontaneous tumor development. *Am. J. Cancer*, 1939, 37, 510-517.
51. GERSHBERG, C. F. Mammary carcinoma in the rat with metastasis induced by oestrogen. *Science*, 1939, 85, 35-37.
52. GUY, G. G. The in-vitro production of transplantable sarcoma from scratch of normal rat fibroblasts maintained in continuous culture. (In press)
53. GUNN, V. Third International Cancer Congress, Atlantic City N. J. 1939, Summaries of Programs, p. 6.
54. GURATI, A. Zelluläre Speicherung cancerogener Kohlenwasserstoffe. *Zschr. f. Krebsforsch.*, 1939, 49, 477-495.
55. HANOW, A. Influence of carcinogenic compounds and related substances on the rate of growth of spontaneous tumors of the mouse. *J. Path. & Bacteriol.*, 1938, 47, 567-579.
56. Idem. Influence of carcinogenic substances on sarcoma induced by the same and other compounds. *J. Path. & Bacteriol.*, 1938, 47, 581-59.
57. HANOW, A. and KOSKOV, A. M. Influence of various polycyclic hydrocarbons on the growth rate of transplantable tumors. *Proc. Roy. Soc. London, Ser. B*, 1937, 31, 447-476.
58. Idem. Association of carcinogenicity and growth inhibiting power in the polycyclic hydrocarbons and other substances. *Proc. Roy. Soc. London, Ser. B*, 1939, 127, 377-387.
59. HIRZIG, I. On the mechanism of carcinogenesis by chemical compounds. *Am. J. Cancer*, 1936, 28, 523-530.
60. HOCHLACHT, C. Further experiments on the effect of carcinogenic hydrocarbons on elimination of Congo red from the circulation. *Am. J. Cancer*, 1940, 39, 365-376.
61. HORMANN, W. J. Hormone therapy of male breast hypertrophy. *Am. J. Cancer*, 1939, 36, 447-51.
62. HOLLANDER, A., COLE, P. A., and BRACKETT, F. S. Absorption and fluorescence spectra in relation to the photochemical action of methylnitrothiuron on yeast. *Am. J. Cancer*, 1939, 37, 364-372.
63. HOLMES, W. C., WILEY, F. H., and WOLFE, H. D. Experimental production of bladder tumors in dogs by administration of beta-naphthylamine. *J. Indust. Hyg. & Toxicol.*, 1934, 30, 40-44.
64. HALL, E. Om 12:56 Dibenzanthracenkarboner Udvikling. *Skrifter stiftet av Kung. Högskola* Food No. 4, Bergen 1937, 141 pages.
65. KACAW, quoted by KINOVA (ref. 68 page 761).
66. KATO, J. G., and KURO, P. Effect of papilloma virus (Shope) upon the ear warts of rabbits. *Proc. Soc. Exper. Biol. & Med.*, 1937, 37, 518-520.
67. KUROKITA, R. Special report, Studies on the carcinogenic chemical substances. *Tr. Soc. Path. Jap.*, 1937, 37, 665-727.
68. LACAMARON, A. Statistique des différents cancers constatés dans les lapins affectés de source, après action prolongée d'hormones oestrogènes. *Bull. de l'Ass. franc. p. l'étude du cancer*, 1938, 37, 66-76.
69. Idem. Sarcomes lymphoïdes apparus chez des souris longuement traitées par des hormones oestrogènes. *Compt. rend. Soc. de biol.*, 1937, 36, 193-195.
70. Idem. Apparition d'adénocarcinomes mammaires chez des souris mâles traitées par une substance oestrogène synthétique. *Compt. rend. Soc. de biol.*, 1938, 36, 64-65.
71. Idem. Relationship of hormones and mammary adenocarcinoma in the mouse. *Am. J. Cancer*, 1939, 37, 434-444.
72. LACAMARON, A. and CHAMBERO, A. Conséquences de l'hypophysectomie chez des souris sujettes au carcinome mammaire, traitées par hormone oestrogène. *Compt. rend. Soc. de biol.*, 1939, 37, 1077-1078.
73. LACAMARON, A. and NYER, W. Différence de réaction de l'hypophyse à l'administration prolongée de substances oestrogènes dans diverses lapines affectées de source. *Compt. rend. Soc. de biol.*, 1937, 36, 2-5.
74. LACAMARON, A. and R. THOM, A. Sur le mécanisme d'une action préventive de la testostérone sur le carcinome mammaire de la souris. *Compt. rend. Soc. de biol.*, 1939, 37, 586-588.
75. LARSENOW, L. T. Endocrine glands in experimental cancer induced by benzopyrene. A study of the endocrine glands in the pathogenesis of tumors. *Am. J. Cancer*, 1940, 38, 494-505.
76. LARA, J. C. Inhibition of growth by 12:56 dibenzanthracene and other agents, etc. *Quart. J. Exper. Physiol.*, 1937, 37, 9.
77. LEWIS, M. W. Methylol inhibitions occurring in the adrenals of animals bearing certain tumors. *Am. J. Cancer*, 1937, 30, 95-10.
78. LOPE, L. and KURT, M. M. Effects of transplants of anterior lobes of the hypophysis on the growth of the mammary gland and on the development of mammary gland carcinoma in various strains of mice. *Am. J. Cancer*, 1939, 36, 56-82.
79. LOPE, L., SCHREIBER, V. and BURKE, E. L. Growth processes induced by estrogenic substances in uterus of mouse. *Am. J. Cancer*, 1938, 34, 413-427.
80. Idem. Changes in the nature of the uterine in vagina, cervix, and uterus of the mouse produced by long-continued injections of oestrogens and by advancing age. *Am. J. Cancer*, 1939, 35, 59-74.
81. LOUDER, E. and STEWART, H. L. Intestinal carcinomas and other lesions in mice following oral administration of 12:56 dibenzanthracene and 30 methylcholanthrene. *J. Nat. Cancer Inst.*, 1940, 30, 7-20.
82. MAGAT, M. A. LEBRON, E. G. and VOUGROUX, D. V. Action of synthetic hydrocarbons on cell growth. *Problems of oncology* Kharkov M. J. 1937, 5-21.

83. MAHO, I. B. and MORTON, J. J. The neoplastic response of dilute brown mice to methylcholanthrene. (In press)
84. MAIST, J., POTIER, A. and PIERRE, G. Influence du propanate de testosterone sur l'évolution du cancer au benzopyrene chez la souris. *Compt. rend. Soc. de biol.*, 1939, 130, 109-112.
85. MAH, I. D. and ROLL, S. Increase in the incidence of lymphomatosis in male fowls by castration. *Am. J. Cancer*, 1939, 30, 315-318.
86. MAY, J. D., W. A., and ROL, I. M. F. Activation of cholesterol by irradiation. *Am. J. Cancer*, 1937, 31, 476-483.
87. MCJUN, I. A., and WOLAVA, W. Effect of 1,2,5,6-dibenzanthracene on spindle cell sarcoma of a rat. *Arch. Pathol.*, 1938, 45, 509-513.
88. MUIR, G. B. and MORTON, J. J. Skin tumors following the single application of methylcholanthrene in C57 brown mice. *Am. J. Pathol.*, 1939, 15, 99-100.
89. Idem. The effect of methylcholanthrene on the latent period of lymphomatosis in dilute brown mice. *Am. J. Cancer*, 1939, 37, 355-363.
90. Idem. The effect of methylcholanthrene on the latent period of breast tumors in dilute brown mice. *Proc. Soc. Exper. Biol. & Med.*, 1939, 42, 583-584.
91. MORTON, J. J. and MITCHELL, R. H. Production of tumors of the prostate of the white rat with 1,2-benzopyrene. *Am. J. Cancer*, 1937, 30, 731-741.
92. MORTON, W. Substances controlling the growth of implanted tumors. *M. J. Australia*, 1937, 2, 105-106.
93. MORTON, J. J. The etiology of cancer in the light of our present knowledge. *Ann. Surg.*, 1937, 106, 530-541.
94. MORTON, J. J., LUCY, C. A., I. M., and MAHO, I. B. The effect of visible light on the development of tumors induced by benzopyrene in the skin of mice. *Am. J. Roentgenol.*, 1940, 43, 848-849.
95. MORTON, J. J., and MUIR, G. B. Some effects of carcinogenic agents on mice subject to spontaneous leukoses. Presented at Third Internat. Cancer Congress, Atlantic City, 1939. (In press)
96. MORTON, J. J. 3,4-Benzopyrene, paraffin, and the production of tumors. *Nature*, 1939, 145, 184-185.
97. Idem. Production of epithelial tumors by irradiation of a preneoplastic skin lesion. *Am. J. Cancer*, 1939, 30, 747-748.
98. Idem. Induction of epithelial tumors by a combination of beta irradiation and painting with benzopyrene. *Am. J. Cancer*, 1938, 30, 56-57.
99. MUIR, G. B. To be published.
100. NAGAI, N. Expositionelle Erzeugung von Harnblasenpapillomen bei Mäusen durch 2-Oxy-1,2-dibenzanthracen. *Beitr. zu krankenpath. und exper. Pathologie*, 1939, 1, 137-140.
101. NAGAI, N., MUIR, G. B., and MORTON, J. J. Effect of 2-Oxy-1,2-dibenzanthracene on the development of the bladder tumor in mice. *Am. J. Cancer*, 1939, 30, 141-144.
102. The effect of 2-Oxy-1,2-dibenzanthracene on the development of the bladder tumor in mice. *Am. J. Cancer*, 1939, 30, 141-144.
103. NAGAI, N. A study of the effect of 2-Oxy-1,2-dibenzanthracene on the development of the bladder tumor in mice. *Am. J. Cancer*, 1939, 30, 141-144.
104. NELSON, W. O. Endometrial and myometrial changes including fibromyomatous nodules induced in the uterus of the guinea pig by the prolonged administration of estrogenic hormone. *Anat. Record*, 1937, 45, 99-107.
105. NICOL, J. I., and REAVES, J. Les cancers provoqués par le méthylcholanthrene chez la souris. *Bull. de l'Ass. franc. p. l'étude du cancer*, 1935, 7, 706-722.
106. OBEILINE, C., GUTTEN, M., and GUTTEN, P. La production expérimentale de tumeurs hypophysaires chez le rat. *Compt. rend. Soc. de biol.*, 1936, 123, 1152-1154.
107. ORR, J. W. The changes antecedent to tumor formation during the treatment of mouse skin with carcinogenic hydrocarbons. *J. Path. & Bacteriol.*, 1938, 46, 405-515.
108. Idem. An investigation of the histological changes in the subcutaneous tissues of mice during the induction of sarcoma by carcinogenic hydrocarbons. *J. Path. & Bacteriol.*, 1939, 46, 157-170.
109. OWEN, S. I., WILSON, H. A., and PRINCE, I. H. Carcinogenesis and growth stimulation. *Science*, 1938, 87, 261-262.
110. PACE, R. C. Cytologic change in the skin of mice during the application of carcinogenic agents. *Arch. Pathol.*, 1938, 20, 800-813.
111. PAPSON, I. D. Changes in the lymph glands of tumor-bearing mice. *J. Path. & Bacteriol.*, 1938, 47, 501-513.
112. PASSER, R. D. Experimental tar tumors in dogs. *J. Path. & Bacteriol.*, 1938, 47, 349-351.
113. PERRY, J. H. The estrogenic activity of 3,4-benzopyrene. *Proc. Soc. Exper. Biol. & Med.*, 1938, 39, 336-347.
114. PERRY, J. H., and LOCKHART, M. S. Experimental production of adenoma of the pituitary. *Am. J. Cancer*, 1939, 35, 4, 2-473.
115. POTIER, J. A. Effect of hard oil, sesame oil, hexachlorocyclopentadiene and 1,2,5,6-dibenzanthracene on certain organs and a transplantable rat sarcoma in animals of pure breed. *Radiology*, 1937, 30, 683-694.
116. PRINCE, I. H., and FLORES, H. W. Proliferation of lymphatics in inflammation. *J. Path. & Bacteriol.*, 1937, 45, 157-170.
117. PYLE, I. C., and MILLER, I. W. A sex difference in the incidence of bladder tumors in mice. *Am. J. Cancer*, 1938, 34, 48-51.
118. REAVES, J. I., DAVIS, A., and MORTON, J. J. Uterine neoplasia induced by the administration of 1,2-dibenzanthracene to the guinea pig. *Am. J. Cancer*, 1938, 30, 683-694.
119. KERR, J. M., and BOSS, G. M. Induction of mammary adenomas in mice of a segregable strain by the synthetic estrone triphenylethylene. *Nature*, 1938, 142, 8.
120. FLORES, H. W. Histology of the bladder in relation to skin cancer. *Am. J. Cancer*, 1938, 30, 4-57.
121. FLORES, H. W. Histology of the bladder in relation to skin cancer. *Am. J. Cancer*, 1938, 30, 4-57.
122. FLORES, H. W. Histology of the bladder in relation to skin cancer. *Am. J. Cancer*, 1938, 30, 4-57.
123. FLORES, H. W. Histology of the bladder in relation to skin cancer. *Am. J. Cancer*, 1938, 30, 4-57.
124. FLORES, H. W. Histology of the bladder in relation to skin cancer. *Am. J. Cancer*, 1938, 30, 4-57.
125. FLORES, H. W. Histology of the bladder in relation to skin cancer. *Am. J. Cancer*, 1938, 30, 4-57.

42. FLAKE, J. and BER, A. Action inhibitrice de Phor mone male sur la formation des cancers, produits par les substances cancérogènes. Bull. de l'Ass. franç. p. l'étude du cancer, 1936, 25: 108-16.
44. FOOTER, L. Production of transplantable carcinoma and sarcoma in guinea pigs by injection of thiostratin. Am. J. Cancer, 1936, 35: 363-373.
45. GARDNER, W. U. Personal communication.
46. GARDNER, W. U., ALLER, E., SARTER, O. M. and STENO, L. C. Carcinoma of the cervix in mice receiving estrogens. J. Am. M. Ass., 1938, 81: 81-85.
47. GARDNER, W. U., KIRSCHBAUM, A., and STENO, L. C. Observations on lymphoid tumors in mice receiving estrogens. Arch. Path., 1940, 39: 7.
48. GARDNER, W. U. Estrogens in carcinogenesis. Arch. Path., 1940, 39: 38-70.
49. GARDNER, W. U. and FREEMAN, C. A. Skeletal changes in mice receiving estrogens. Proc. Soc. Exper. Biol. & Med., 1938, 37: 678-679.
50. GARDNER, W. U., STENO, L. C., and SARTER, O. M. The mammary glands of mature mice of strains which vary in susceptibility to spontaneous tumor development. Am. J. Cancer, 1939, 37: 510-517.
51. GERSHBERGER, C. F. Mammary carcinoma in the rat with metastases induced by estrogen. Science, 1936, 80: 34-37.
52. GUY, G. O. The *in vitro* production of transplantable sarcoma from strains of normal rat fibroblasts maintained in continuous cultures. (In press.)
53. GUTER, V. Third International Cancer Congress, Atlantic City N. J., 1939, Summaries of Program, p. 6.
54. GRANT, A. Zelluläre Speicherung onkologischer Kohlenwasserstoffe. Ztschr. f. Krebsforsch., 1939, 49: 477-495.
55. HADROW, A. Influence of carcinogenic compounds and related substances on the rate of growth of spontaneous tumors of the mouse. J. Path. & Bacteriol., 1938, 47: 567-579.
56. Idem. Influence of carcinogenic substances on sarcoma induced by the same and other compounds. J. Path. & Bacteriol., 1938, 47: 58-59.
57. HADROW, A., and ROBINSON, A. M. Influence of various polycyclic hydrocarbons on the growth rate of transplantable tumors. Proc. Roy. Soc. London, Ser. B, 1937, 22: 447-476.
58. Idem. Association of carcinogenicity and growth inhibiting power in the polycyclic hydrocarbons and other substances. Proc. Roy. Soc. London, Ser. B, 1939, 27: 477-487.
59. HANSEN, I. On the mechanism of carcinogenesis by chemical compounds. Am. J. Cancer, 1936, 28: 532-539.
60. HOCK LAMM, C. Further experiments on the effect of carcinogenic hydrocarbons on elimination of Congo red from the circulation. Am. J. Cancer, 1940, 39: 365-376.
61. HOFFMAN, W. J. Hormone therapy of male breast hypertrophy. Am. J. Cancer, 1936, 30: 247-51.
62. HOLLANDER, A., COLE, P. A., and BRACKETT, F. S. Absorption and fluorescence spectra in relation to the photochemical action of methylcholanthrene on yeast. Am. J. Cancer, 1939, 37: 264-272.
63. HUIJER, W. C., WILLY, F. H., and WOLFE, H. D. Experimental production of bladder tumors in dogs by administration of beta-naphthylanthrene. J. Indust. Hyg. & Toxicol., 1934, 20: 46-64.
64. HILAL, E. On 1236 Dibenzanthracene. Utvikling Skriftet utgitt av Klaus Hansens Food No. 24, Bergen, 1937, 143 pages.
65. KAGAW, quoted by Kikuchi (ref. 68 page 705).
66. KING, J. G., and ROOS, P. Effect of papilloma virus (Shope) upon the ear warts of rabbits. Proc. Soc. Exper. Biol. & Med., 1937, 37: 518-520.
67. KUROKI, R. Special report. Studies on the carcinogenic chemical substances. T. Soc. Path. Jap., 1937, 37: 663-737.
68. LACABARRE, A. Sémiologie des différents cancers constatés dans les ligues sélectionnées de souris, après action prolongée d'hormones oestrogènes. Bull. de l'Ass. franç. p. l'étude du cancer, 1938, 27: 66-6.
69. Idem. Sarcomes lymphoïdes apparus chez des souris longuement traitées par des hormones oestrogènes. Compt. rend. Soc. de biol., 1937, 30: 82-104.
70. Idem. Apparition d'adénocarcinomes mammaires chez des souris mâles traitées par une substance oestrogène synthétique. Compt. rend. Soc. de biol., 1938, 30: 64-643.
71. Idem. Relationship of hormones and mammary adenocarcinomas in the mouse. Am. J. Cancer, 1939, 37: 414-444.
72. LACABARRE, A. and CRANFORD, A. Conséquences de l'hypophysectomie chez des souris sujettes au carcinoma mammaire, traités par hormones oestrogènes. Compt. rend. Soc. de biol., 1939, 31: 1077-078.
73. LACABARRE, A. and NIXE, W. Différence de l'action de l'hypophyse à l'administration précoce de substances oestrogènes dans diverses ligues sélectionnées de souris. Compt. rend. Soc. de biol., 1937, 30: 2-5.
74. LACABARRE, A. and RAUJAT, A. Sur le mécanisme d'une action préventive de la testostérone sur le carcinoma mammaire de la souris. Compt. rend. Soc. de biol., 1939, 31: 506-553.
75. LARKEOW, L. T. Endocrine glands in experimental cancer induced by benzo(a)pyrene. A study of the endocrine glands in the pathogenesis of tumor. Am. J. Cancer, 1940, 38: 492-505.
76. LEIN, J. C. Inhibition of growth by 1236 dibenzanthracene and other agents, etc. (Quart. J. Exper. Physiol., 1937, 37: 162-92).
77. LEVIN, M. R. Myeloid infiltrations occurring in the adrenals of animals bearing certain tumors. Am. J. Cancer, 1937, 30: 99-100.
78. LOPEZ, L., and LLOYD, M. M. Effects of transplant of anterior lobes of the hypophysis on the growth of the mammary gland and on the development of mammary gland carcinoma in various strains of mice. Am. J. Cancer, 1939, 35: 90-82.
79. LOPEZ, L., SUTHERLAND, V., and BUNICK, E. L. Growth processes induced by estrogenic substances in glands of mouse. Am. J. Cancer, 1938, 34: 413-437.
80. Idem. Changes in the nature of the uterus in vagina, cervix, and uterus of the mouse produced by long-continued injections of estrogens and by advancing age. Am. J. Cancer, 1939, 35: 36-474.
81. LOWERY, E., and STEWART, H. L. Intestinal adenomas and other lesions in mice following oral administration of 1236 dibenzanthracene and 3-methylcholanthrene. J. Nat. Cancer Inst., 1940, 3: 40.
82. MAGAT, M., A. LEHNER, E. G., and VOLKHOV, D. V. Action of synthetic hydrocarbons on cell growth. Problems of oncology. Kharkov M. J. 1937, 3-22.

- 83 MAHONEY, I. B. and MORTON, J. J. The neoplastic response of dilute brown mice to methylcholanthrene. (In press.)
- 84 MAISI, J., POIRBAIX, A., and RIJCKHAERT, G. Influence du propionate de testostérone sur l'évolution du cancer au benzopyrène chez la souris. *Compt. rend. Soc. de biol.*, 1939, 130, 109-112.
- 85 MARI, I. D., and ROSIN, S. Increase in the incidence of lymphomatosis in male fowls by castration. *Am. J. Cancer*, 1940, 39, 315-318.
- 86 MAYNORTH, W. A., and ROE, J. M. I. Activation of cholesterol by radiation. *Am. J. Cancer*, 1937, 31, 476-483.
- 87 McJANE, I. A., and WOLANIN, W. Effect of 1,2,5,6-dibenzanthracene on spindle cell sarcoma of a rat. *Arch. Path.*, 1935, 25, 506-513.
- 88 MIDGE, G. B., and MORTON, J. J. Skin tumors following the single application of methylcholanthrene in C 57 brown mice. *Am. J. Path.*, 1939, 15, 209-302.
- 89 Idem. The effect of methylcholanthrene on the latent period of lymphomatosis in dilute brown mice. *Am. J. Cancer*, 1939, 37, 355-363.
- 90 Idem. The effect of methylcholanthrene on the latent period of breast tumors in dilute brown mice. *Proc. Soc. Exper. Biol. & Med.*, 1939, 42, 583-584.
- 91 MOORE, R. A., and MICHONNA, R. H. Production of tumors of the prostate of the white rat with 1,2-benzopyrene. *Am. J. Cancer*, 1937, 30, 731-741.
- 92 MORTON, J. J. Substances controlling the growth of unplanted tumors. *M. J. Australia*, 1937, 2, 1005-1006.
- 93 MORTON, J. J. The etiology of cancer in the light of our present knowledge. *Ann. Surg.*, 1937, 106, 539-561.
- 94 MORTON, J. J., LUCE CLAUSEN, I. M., and MAHONEY, I. B. The effect of visible light on the development of tumors induced by benzopyrene in the skin of mice. *Am. J. Roentgenol.*, 1940, 43, 896-898.
- 95 MORTON, J. J., and MIDGE, G. B. Some effects of carcinogenic agents on mice subject to spontaneous leukoses. Presented at Third Internat. Cancer Congress, Atlantic City, 1939. (In press.)
- 96 MORTON, J. J. 3,4-Benzpyrene, pyramoxium and the production of tumors. *Nature*, 1940, 145, 184-185.
- 97 Idem. Production of epithelial tumors by irradiation of a pre-cancerous skin lesion. *Am. J. Cancer*, 1947, 39, 746-748.
- 98 Idem. Production of epithelial tumors by a combination of beta radiation and painting with benzopyrene. *Am. J. Cancer*, 1938, 4, 76-84.
- 99 MORTON, J. J. Personal communication.
- 100 NAGAO, S. Experimentelle Erzeugung von Harnblasenpapillomen durch Fütterung des 4-Oxy-1,2,5,6-dibenzanthracen. *Arch. Path. & Bacteriol.*, 1937, 48, 99-102.
- 101 NIELSEN, W. O. Endometrial and myometrial changes including fibromyomatous nodules induced in the uterus of the guinea pig by the prolonged administration of estrogenic hormone. *Anat. Record*, 1937, 48, 99-102.
- 102 NICOD, J. P., and KECARF, J. Les cancers provoqués par le méthylcholanthrène chez la souris. *Bull. de l'Ass. franc. p. l'étude du cancer*, 1935, 27, 706-712.
- 103 OBERLING, C., GUÉPIN, M., and GUÉPIN, P. La production expérimentale de tumeurs hypophysaires chez le rat. *Compt. rend. Soc. de biol.*, 1936, 123, 1152-1154.
- 104 ORF, J. W. The changes antecedent to tumor formation during the treatment of mouse skin with carcinogenic hydrocarbons. *J. Path. & Bacteriol.*, 1938, 46, 493-515.
- 105 Idem. An investigation of the histological changes in the subcutaneous tissues of mice during the induction of sarcoma by carcinogenic hydrocarbon. *J. Path. & Bacteriol.*, 1939, 49, 157-170.
- 106 OWEN, S. I., WILKS, H. A., and FRISCH, I. H. Carcinogenesis and growth stimulation. *Science*, 1938, 87, 261-267.
- 107 PAGE, R. C. Cytologic change in the skin of mice during the application of carcinogenic agents. *Arch. Path.*, 1938, 6, 800-813.
- 108 PAPSON, I. D. Changes in the lymph glands of tumor-bearing mice. *J. Path. & Bacteriol.*, 1938, 47, 501-523.
- 109 PASSY, R. D. Experimental tar tumors in dogs. *J. Path. & Bacteriol.*, 1938, 47, 349-351.
- 110 PERRY, I. H. The estrogenic activity of 1,4-benzopyrene. *Proc. Soc. Exper. Biol. & Med.*, 1938, 30, 346-347.
- 111 PERRY, I. H., and LOCHHEAD, M. S. Experimental production of adenoma of the pituitary. *Am. J. Cancer*, 1939, 35, 47-53.
- 112 POLIA, J. A. Effect of lard oil, sesame oil, turpentine and 1,2,5,6-dibenzanthracene on certain organs and a transplantable rat sarcoma in animals of pure breed. *Radiology*, 1937, 9, 683-694.
- 113 PRINCE, B. D., and LOFFLY, H. W. Proliferation of lymphatics in inflammation. *J. Path. & Bacteriol.*, 1937, 45, 157-170.
- 114 PYLES, I. C., and MILLER, I. W. A sex difference in the incidence of bone tumors in mice. *Am. J. Cancer*, 1938, 34, 745-751.
- 115 REICHERT, M., DASSI, A., and MORRIS, I. L. Effet du radium sur le processus d'élimination des hydrocarbures cancérigènes métaboliques. *Tumors*, 1939, 13, 645-647.
- 116 ROUSE, J. M., and BOSSER, G. M. Induction of mammary carcinoma in mice of a susceptible strain by the synthetic estrogen triphenylethylene. *Nature*, 1938, 14, 587.

24. R. W. TEEB, L. G. LAMSTER, J. and STERNBERG, A. Neoplasms in albino rats resulting from the feeding of crude heat germ oil made by ether extraction. *Proc. Soc. Exper. Biol. & Med.* 937 96 424-426
25. R. W. TEEB, H. P. and B. M. C. A. Tumor production in mice. Ith ultraviolet irradiation. *Am. J. Cancer* 930, 33 45-62.
26. SCHMIDT, H. O. Die Wirkung bestrahlten ergosterins und verwandter Stoffe auf Epithelien etc. *Zschr. f. Krebsforsch.* 937 43 335-346.
27. BELLER, F. R. Tumors in rats and mice following the injection of thorotrast. *Brit. J. Exp. Path.* 938 9 60-67
28. SPRIGMAN, A. M., SIEG, R. M. J. and AURANTER, L. Experimental production of brain tumors in mice. Ith methylcholanthrene. *Am. J. Cancer* 930, 37 364-369
29. SEMPERON, A. and MORELLI, E. Carcinomas of the kidney in rats treated. Ith beta anthracenolines. *Am. J. Cancer* 930, 33 334-337
30. SELLAN, M. J. Studies in carcinogenesis. I. Methyl derivatives of 3 benzopyrene. *Am. J. Cancer* 935, 21 409-417
31. SELLAN, M. B. Production of lung tumors in mice by intratracheal administration of carcinogenic hydrocarbons. *Am. J. Cancer* 930, 33 338-342
32. SOWERS, H. and BLOCK, E. Urine excretion in cancer. *Am. J. Cancer* 930, 33 30-34
33. SCHREIBER, V., BLUMCOCK, R. S. and LORR, L. The development of sarcoma in mice following long continued injections of buffered solution of hydrochloric acid. *Am. J. Cancer* 930, 39 50-60.
34. IDEM. Reversibility of hyalinization in the mouse uterus produced by injections of estrogen and the changes in the mammary gland and ovaries after cessation of injections. *Am. J. Cancer* 930, 38 7-13
35. TAKEMURA, H. Ueber die Freisetzung der Mammakarzinome durch die subcutane Injektion der Konzentrierten Zuckermolasse. *Gann* 930, 33 93-95
36. T. CASO, J., COOPER, Z. K., and SELLAN, M. G. The effect of light on benzopyrene cancer in mice. *Surg., Gynec. & Obst.* 933, 66 980-993
37. T. ALER, A. and MORELLI, E. L'influence de la castration ovarienne sur le développement et la croissance des tumeurs du goudron. *Compt. rend. Soc. de Biol.* 937, 5 70-8
38. TROUSSER, C. W. Hormonal interrelations between reproduction, mammary gland growth and lactation. *Growth* 930, 3 3-35
39. T. ORT, J. M. and T. ORT, C. C. Further observations on the organs of mice palated with carcinogenic agents. *Am. J. Cancer* 937 39 78-92
40. VALADE, P. Recherches sur l'acétide carcinogène du méthylcholanthrène. *Bull. de l'Ass. franç. p. l'étude du cancer* 937 26 43 46
41. V. G. LEE, P. J. and KORTI, G. R. Sexuality, fertility, follicular hormone and disposition to mammary cancer in female mice. *Am. J. Cancer* 930, 38 500-515
42. ORT, J. M., F. and CURRIE, L. Effect of hormones upon cells grown in vitro. Effect of sex hormones upon fibroblasts. *Am. J. Cancer* 930, 30 350-353
43. WARREN, F. L. Estimation of iron in the hamph glands of mice during the tumor. Ith carcinogenic compound. *Bio-Chem. J.* 930, 33 780-783
44. W. TERMAN, V. Cancer expérimental de l'estomac son rapport avec la genèse du cancer de l'estomac humain. *Acta union Internat. contre cancer* 1930, 4 764-767
45. WELT, A. Experimental production of tumors in beagle of hite rats. *Arch. Path.* 935, 26 777-780
46. WELT, J. and WELT, A. A. Inhibition of growth of the rat by oral administration of methylcholanthrene, benzopyrene or pyrene and the effects of various dietary supplements. *J. Biol. Chem.* 930, 3 140-6
47. WIDOWSKA, F. M. P. Presence of cancer-producing substances in roasted food. *Nature* 930, 143 684
48. WOODROW, W. H. Vent and soil in experimental carcinogenesis. *Am. J. Cancer* 933, 3 447-451
49. WOODROW, S. B. Responses of carcinogenic hormones administered to tumor formation. *Am. J. Path.* 937 3 663-669
50. WOLFE, J. M., BRACK, E., and WINGARD, A. W. The estrous cycle and associated phenomena in strain of rats characterized by high incidence of mammary tumors together with observations on the effects of ad. and androg. are on these phenomena. *Am. J. Cancer* 930, 38 383-393
51. WOLFE, J. M. and HARTLEY, J. B. Action of testosterone propionate on the structure of the anterior pituitary of the female rat. Ith particular reference to the effects of prolonged administration on the level of cells. *Endocrinology* 930, 5 372-384
52. WOLFE, J. M., and WINGARD, A. W. Histologic effects induced in the anterior pituitary of the rat by prolonged injection of estrin. Ith particular reference to the production of pituitary adenoma. *Endocrinology* 935, 3 300-310
53. WOODLEY, G., DEARIE, F. and LITTLE, C. C. Mammary tumor development in mice as ascertained at birth. *Proc. Nat. Acad. Sci.* 930, 5 277-279
54. ZONDEL, B. Hypophyseal tumors induced by estrogens. *Am. J. Cancer* 935, 21 555-559

# NEUROGENIC SARCOMA

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THE term sarcoma imparts a distinct and well understood meaning. The word neurogenic creates the thought of arising from nerve tissue. When these two words are put together implying a name, inaccuracy and probably confusion results. Sarcoma must originate from tissues that have a mesodermic origin. Nerve tissue begins in another layer, the ectoderm. Hence, the inaccuracy of the title. Furthermore, the recognized source of neurogenic sarcoma is from the sheaths of the central and peripheral nerve trunks or fibers and not from nerve tissue. However, the title, though oddly coupled, has the advantage of being well established. It also creates in our minds two valuable ideas: first, the disease is malignant, second, it specifies the geography of the disease, the areas and structures where such an entity might be suspected.

We, as clinicians, may properly overlook discrepancies in terminology, once they are understood. Our task is to become familiar with the etiology, symptomatology, and therapy of an interesting subject, neurogenic sarcoma.

The etiology of neurofibromas, neurofibromatosis or von Recklinghausen's disease is unknown. So too is the cause of neurogenic sarcoma unknown. All of these arise from the connective tissue coverings of nerves. There are some who believe that neurogenic sarcoma always arises from the sheath of Schwann. The embryological origin of this sheath compared to the origin of the other coverings of nerves, cranial or peripheral, and the tumors which arise from them has been thoroughly discussed by Penfield, Stout, and Geschickter.

Many are of the opinion that a solitary tumor called neuroma or neurofibroma may be a single manifestation of a disease which at times is capable of producing multiple tumors. And further, postmortem examination may reveal that there had existed a fibromatosis involving hidden nerve tissue. The author suggests that one who wishes to familiarize himself with the interesting subject of neurofibromatosis in a comprehensive manner

should obtain Thomson's monograph, *Neuroma and Neurofibromatosis*<sup>1</sup>

Neurogenic sarcoma has been found in practically every area and organ of the body. Such extensive distribution of a disease not only signifies its importance but increases the multiplicity of signs and symptoms that can accompany it. The alertness of the clinician is ever necessary if diagnostic errors are to be avoided. It must be admitted, however, that few of these tumors are properly labeled prior to exploration or biopsy, and then often with difficulty. The reasons apparently for mistakes with this disease are: First, it is not common. No doubt it is more frequent than suspected. Second, its rarity naturally causes the observer to direct his attention to the organ producing the symptoms—stomach, intestine, lung, brain, spinal cord. Third, intracranial or motor and sensory symptoms, pain included, suggest a more frequent condition than neurogenic sarcoma. The visible or palpable tumor calls to mind a more common type of lump.

It must not be inferred that just because skin manifestations are not present, a visible or palpable lump cannot be a sarcoma of nerve sheath origin. Many occur, though diagnosed as a more frequently seen tumor and operated on as such, followed frequently with recurrence.

CASE 1. C.S., No. 53,581, a white woman, aged 43, was seen January 6, 1938. The patient was referred to us because of a tumor of the upper left side of the chest. She said this began as a birthmark which was a flat red spot about 2 inches wide. She also said that there was a spot on this red area which seemed to be a wart, which 17 years before had been opened by accident. Bleeding occurred. It began to grow larger following this injury, and after 3 years was operated upon and supposedly removed. On January 21, 1924, the pathological report described a myomatous growth on shoulder, soft and microscopically on border line between myoma and nonmetastasizing spindle cell sarcoma. She also had an abdominal operation at this time. Two years later, the growth was about the size of a walnut and was again removed by the same surgeon. On July 6, 1926, the pathological report described a subepithelial proliferation of fibrous tissue with much production of collagen typical of keloid. Five years ago she had a thyroidectomy and the recurrent tumor was again removed by another surgeon. No pathological report was obtainable. Two years ago, she noticed the tumor growing again. She had lost some weight. She had been dieting.

On examination we saw on the anterior portion of the left shoulder (Fig. 1) a growth and also a scar. Both

<sup>1</sup>The Surgeon General's Library of Washington D.C. was kind enough to loan the author a copy of this book through the King County Medical Library, Seattle.

From the Tumor Clinic, King County Hospital (Formerly Harborview).

Presented in the Cancer Symposium before the Clinical Congress of the American College of Surgeons, Chicago, October 21-25, 1940.



Fig. 1.

Fig. 1. Case . . . The tumor began as birthmark. It was removed three times, recurring after each operation.

Fig. 2.

Fig. 2. Case . . . Gross specimen removed with castery skin graft as necessary.

measured about 5 by 3 centimeters. This was large tumor 5 by 3 centimeters, and raised above the level of the skin 4 centimeters. There was bluish cast to the most prominent part of the mass. Behind this and above it was reddish spot which seemed incorporated in the scar. At the lower margin of the scar there was another reddish area which seemed more like growth. It was slightly tender. The rest of the scar was white. The scar was movable on the chest wall. There were no enlarged nodes in the axillary, cervical or suprascapular areas.

At operation the tumor mass including all of the surrounding scar was dissected widely down to the fascia of the pectoral major muscle (Fig. 1). The fascia of that muscle was removed with the described tissue. Several

large vessels were encountered approaching the mass in the subcutaneous tissue. These were ligated at distance. The castery was used throughout. The wound could not be closed, hence the area was covered with black skin graft.

In microscopic sections of this nodule there was section composed of collagenous, firm, fibrous tissue, moderate vascular enclosing the nodule described grossly. The latter was composed of haphazardly arranged bands and cords of reticular fibers packed with cells, the nucleus and cytoplasm of which were indistinct, but the nuclei were prominent, round to spindle-shaped. Some of the nuclei were larger and more active than others but in no place was there any evidence of malignancy.

**Diagnosis:** Fibroma. Sections stained with Masson trichrome technique and with an Giemsa, show that there is much collagen material between the fibroblastic type of cells. This is fibromyoma and can be called nerve fibromyoma, but it is not nerve sheathed tumor (Fig. 3).

This case apparently was not microscopically a neurogenic sarcoma, but its repeated recurrence shows that it was clinically malignant.

**CASE FG No 6408.** *White male, aged 55, seen August 9, 1934.* The patient came to the clinic with tumor of the right upper arm, inner side. It had been gradually increasing in size. He first noticed this lump by accident 4 or 5 years ago. A year ago, he noticed kind of numb pain with itching of the hand. There had been aching pain in the arm since last April.

The patient presented tumor on the under surface of the upper arm that encroached upon the posterior axillary fold. It was about 4 centimeters in length and 7 centimeters in diameter. It was fairly soft and slightly tender. It was more tender when one pressed it upon the under surface of the arm along the level of the nerves and vessels than it was from bilateral compression. It was rather soft and compressible. When the patient was directed to bend the triceps muscles part under tension, this tumor came markedly to the surface and became hard. There were no palpable nodes in the axilla. The grip of both hands was about the same. He was unable to recognize

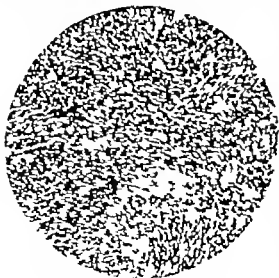


Fig. 3. Case . . . Photomicrograph of fibromyoma or neurofibroma.



Fig 4

Fig 4 Case 2 Age, 55 years The patient first noticed a lump 4 or 5 years ago on the under side of the upper arm. A year ago, he noticed pain with itching of the hand. The tumor is 7 centimeters in length and 5 centimeters in diameter. It is fairly soft and tender. It is more tender when one presses upon the under surface along the level of

a difference in pulse. The mass did not pulsate. The tumor was removed.

At the operation, it was found, after the tumor was exposed, that a large nerve entered the proximal end of the tumor as shown in Figure 5, but its identification was lost in the tumor wall, however, it emerged as a nerve strand distal to the tumor. It was necessary to sacrifice this nerve. The patient has been seen recently and there is no evidence of recurrence.

A diagnosis of neurofibroma, benign, was made August 11, 1934 (Fig 4, 5, 6).

**Pathological report** This is a soft, egg shaped structure, 15 centimeters long and 7 centimeters in diameter. It is covered with a smooth sheet of membrane like tissue and from it, apparently incorporated in the wall, are several cord like structures resembling nerves. Sectioning reveals the structure as a cyst like formation with a soft wall from 0.5 to 1 centimeter thick, composed of soft, quasi translucent, pale yellow brown tissue. To the lining are adherent small collections of glistening, greasy, semicrystalline yellow brown material, and the cavity contains about 50 cubic centimeters of thick, greasy, glittering, pale yellow fluid.

Microscopic examination revealed adherent to the lining a much necrotic, largely amorphous material arranged in a pattern of many angular clear spaces, from which some crystalline material has presumably been dissolved out, microscopic examination of the fluid content revealed cholesterol crystals. Beneath the lining, the wall was formed by dense fibrous tissue, in places hyalinized, in places heavily infiltrated with lymphocytes and plasma cells. Deeper still the tissue was of much softer texture and formed by small round and oval cells with nuclei about 10 microns in diameter, surrounded by clear spaces and a small peripheral membrane so that the general pattern was that of nerve tissue, these cells resembled myelinated nerve fibers, interlaced with them in many places were thin spindle cells resembling fibroblasts. There was also in this part of the wall a heavy infiltration of lymphocytes around some of the blood vessels. Nothing resembling ganglionic cells could be identified.

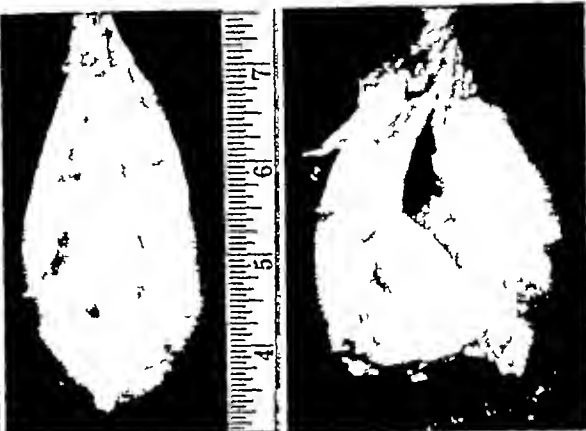


Fig 5

the nerves and vessels than it is on the opposite or posterior surface. It is soft and compressible. The tumor was removed June 11, 1934, with cautery. The pathological report was neurofibroma, benign. He has been seen recently with no evidence of recurrence.

Fig 5 Case 2 Gross tumor involving the radial nerve

Finding a single neurofibroma of a large nerve trunk prompts the constant watch for the appearance of others.

The literature is replete with caution (Adair, Pack, and especially Ewing), to the surgeon that the removal of such a tumor requires preparation for radical surgery. Nerve roots entering or attached must be severed with a wide margin to avoid recurrence. Stewart has called our attention to the fact that extension from the tumor

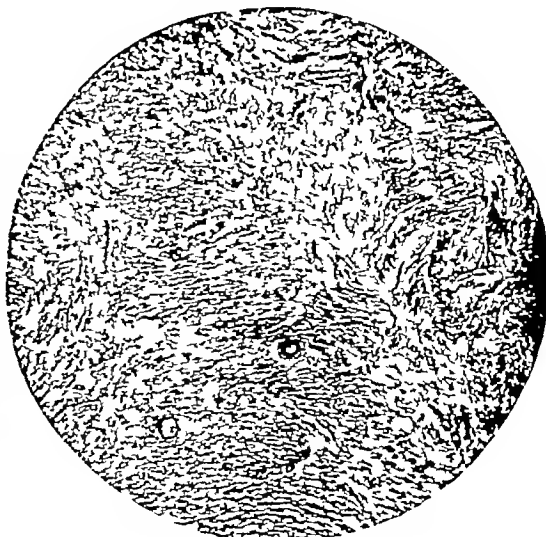


Fig 6 Case 2 Photomicrograph of a neurofibroma





Fig. 7

Fig. 7. Case 3. Over the patient's body are scattered discreet papilloma-like tumors which arose from the skin. None are pedunculated. She stated that she has had these all her life. They are compressible and tender.

Fig. 9. Case 3. A found tumor mass on the inner side of the left leg, at the level of the left knee joint of which the patient complained. This is a smooth, globular tumor



Fig. 9

mass 6 centimeters in diameter which had localized tenderness. There is brownish color over it such as similar to other spots on her body. This mass is firmly attached to the structures of the internal surfaces of the knee joint. The mass is quite firm, compressible and partially movable. There are areas of pigmentation all over the body. These areas are of different size

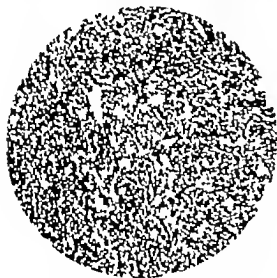


Fig. 8. Case 3. Photomicrograph of tumor seen in Figure 9. Neuroglial sarcoma.

may readily proceed within the nerve sheaths some distance from its origin. The nerve trunk may not be larger than normal, but it should be severed far beyond the growth. Large blood vessels similarly associated with the growth are ligated as far away as possible.

Multiple neurofibromas are more commonly found on the surface of the body. They are variable in size. The shape usually is spherical or ovoid. They may be pedunculated or sessile. Some are palpable in the deeper layers of the skin. The newer ones apparently are pinkish in color while the older ones take on the color of the surrounding skin or are paler as if time had deprived them of the blush of young vascularity. The surface of the skin in these individuals is usually pigmented, ranging from that of small freckles scattered indiscriminately to larger rounded, and irregular patches of darker or light brown color. The great majority of these abnormalities are painless.

The history records that these tumors be-

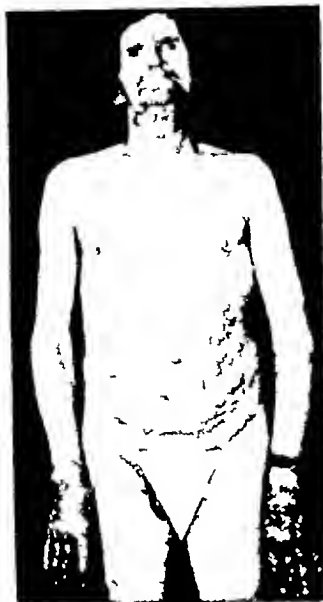


Fig 10

Fig 10 Case 4 The patient, aged 66, has multiple tumors over the skin of the body. Two months before coming to the clinic in September, 1933, one posterior to the right ear became ulcerated and increased rapidly in size. It had been cut by his barber several months previously and had not healed.



Fig 12

Fig 12 Case 4 Generalized skin manifestation of von Recklinghausen's disease. One growth on the neck ulcerated.

gan in early childhood and have gradually increased in number and size as the years passed. The patient has become accustomed to his abnormal skin, and he considers it not worthy of complaint.

Many observers (Ewing) have mentioned that accompanying the skin manifestations of this disease, occasionally neoplastic changes exist on deeper nerve trunks. They may involve both motor and sensory groups. Pain or other sensations naturally follow the involvement of tracks which are sensory in nature. Craig emphasizes this symptom.

One of our patients (Case 3) was seen because she began having the appearance of a lump and pain, although for years, there had been multiple lumps in her skin.

CASE 3 I V No. 22,030, a white woman, aged 42, was seen March 3, 1932. The patient had a swelling of the inner surface of the left knee. The swelling had become painful radiating to the foot. She noticed a mass about a year ago and it had grown since then.

Examination revealed over the patient's body scattered discrete papillomatous looking tumors which arose from the skin. None of the papillomas were pedunculated. She stated that she had had these all her life. They were compressible and tender (Fig 7). We found a tumor mass on the inner side of the left leg at the level of the left knee

joint of which the patient complained (Fig 9). This was a smooth, globular tumor mass 16 centimeters in diameter which possessed localized tenderness. There was a brownish color over it which was similar to other spots on her body. This mass was firmly attached to the structures of the internal surfaces of the knee joint. The mass was quite firm, compressible, and partially movable. There were

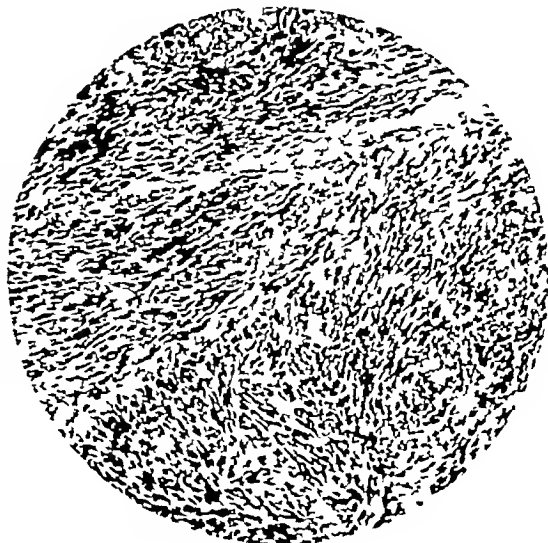


Fig 11 Case 4 Neurofibroma or neurogenic sarcoma



Fig. 3. Case 5. Von Recklinghausen's disease with malignant change.

areas of pigmentation all over the body. These areas were of different size. A cautery excision of the tumor *in situ* as performed by the author March 5, 1932. A portion of the hamstring group was sacrificed in separating the tumor at the upper portion. The tumor was definitely encapsulated and appeared to be in intimate contact with sensory nerve root passing into or fraying out to the tumor. On subsequent visits, there was found lymphedema of the lower leg which disappeared later. When last seen 3 years later there was no evidence of recurrence.

At operation, a round tumor of the leg, 3 centimeters in diameter, thinly encapsulated. On one side the capsule was firmly adherent to the muscle fascia. On dissection, the central portion consisted of peaty-like necrotic material. The tumor substance was soft, friable, and actively proliferating at the surface. The gross diagnosis was necrotizing sarcoma (Fig. 4).

Microscopic examination showed that the tumor consisted of moderate sized spindle cells and fairly numerous mononuclear giant cells. Mitoses was prominent.



Fig. 5. Case 5. Roentgenogram showing von Recklinghausen's disease with bone involvement.

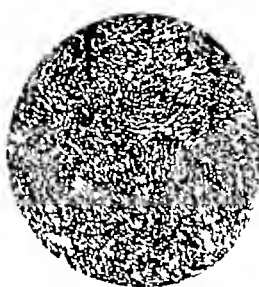


Fig. 4. Case 5. Von Recklinghausen's disease showing neurogenic sarcoma. One of the multiple tumors removed to complete the record. It is a neurofibroma.

Diagnosis: Possible rhabdomyosarcoma, or neurogenic sarcoma.

On August 9, 1932, tumor was found over the twelfth thoracic vertebra. A small piece of tissue was removed from the back. The piece of skin, 4.5 by 4 centimeters in size, in the center of it was papillomatous growth, 1 centimeter in diameter. Immediately underneath the papillomatous growth was tumor mass, 1 centimeter by 1 centimeter.

The diagnosis was neurofibroma. (Taken to complete the record.)

The lump, interestingly enough, of which the patient complained, was fortunately superficial and palpable. Had it arisen from a nerve trunk more deeply situated, and had she not had skin manifestations to offer a clue toward a diagnosis, she doubtless would have been subjected to a number of imaginative procedures for diagnosis, emphasizing again the statement that symptoms with pain which are not diagnosed by modern procedures may (with merit) suggest this disease.

This patient had neurogenic sarcoma associated with von Recklinghausen's disease. She was seen 3 years later with no evidence of recurrence. Such a patient should be informed by her physician that her disease may again produce tumor of malignant type.

The most important clinical significance of von Recklinghausen's disease is that malignant changes do occur. This change may be exemplified by local recurrence following the removal of what was thought to be a benign tumor. The intimate association of such a lesion with a nerve should

warn the surgeon that the removal of this growth must be complete with a wide margin, else as has been warned by Ewing, Hosoi, and others, a recurrence is apt to appear, the eradication of which is more difficult and more mutilating than apparent at the first operation. Hosoi states

"In résumé, malignant transformation takes place in about 13 per cent of all cases of von Recklinghausen's disease. When this happens, the tumor grows rapidly and tends to recur locally even after repeated operative measures. Metastasis is usually late and frequently absent, but may rarely occur early. In some cases, the mere extirpation of a malignant tumor or even a benign one appears to stimulate another neurofibroma distantly located to undergo sarcomatous transformation. Prognosis is very poor, the patient succumbing to cachexia and postoperative complications if not to the metastasis."

For emphasis, I further quote his remarks reporting recorded cases of malignant change in neurofibromatosis

"According to Garre, there is a striking tendency to sarcomatous transformation in multiple neurofibromatosis, for in at least 12 per cent of all cases this sarcomatous change takes place from a benign neurofibroma. Garre calculated this percentage on the basis of 17 collected cases.

Using the 1927 figures of Fischer, when he collected reports of 466 cases of von Recklinghausen's disease, one obtains an incidence of malignant changes of about 13 per cent which is in agreement with Garre. These neurosarcomas have been observed more frequently in the deeper nerve trunks.

"Ewing stated that the serious nature of these deeper tumors is very imperfectly realized by most surgeons, so that the number of victims of this disease is much larger than is generally believed. He added that the primary attack on these tumors must be undertaken with great caution."

Adair's practical article on neurogenic sarcoma so frequently associated with this disease is one of the few which offers suggestions for the therapy of these tumors.

Westphalen reported a case of multiple fibromas of the skin, nerves, and ganglia, one of which in the fifth cervical nerve underwent a sarcomatous change.

"In their cases of [from Hosoi] multiple neurofibromatosis, Campana described a sarcomatosis of the skin, Sorger, a sarcoma of the axilla, Gernet, a sarcomatous transformation of a massive plexiform fibroma of the shoulder and upper part of the arm, Heydeweller, a fibrosarcoma of the right popliteal space, Feindel, a sarcoma globocellulare of the leg, and Gluge, a sarcoma in the pelvis, the size of a child's head.

"In Cimmino's case, a large sarcoma in the sacral region was associated with about 450 fibromatous tumors of the skin. Jeanselme and Orillard reported a case of fibrosarcoma of the saphenous nerve with elephantiasis molle congenita of the overlying skin. Adrian found at necropsy a fibrosarcoma of the duodenum which was associated with multiple fibromas of the skin and internal viscera and a neuromyxoma in the supraclavicular fossa about the size

of a child's fist. In MacKenzie's case, in addition to the multiple soft tumors in the skin, a good egg sized sarcoma of the sciatic nerve was observed. Shouldice reported a case of multiple peripheral fibromas in which operation disclosed dozens of small tumors about the size of millet seeds all over the stomach and a fibromyxosarcoma on the greater curvature of the stomach."

Ten to fifteen per cent of neurogenic sarcomas are associated with neurofibromatosis—von Recklinghausen's disease—and are the ones most frequently diagnosed. The physician recognizes this association as an important clue. When, however, a deep seated tumor is found in such a patient, the thought—appreciating its location—that it might be a neurogenic sarcoma should be kept in mind, or if the tumor is superficial, larger than others, growing or producing symptoms, its diagnosis is more likely.

CASE 4 D.E., No 52,659, a white male, aged 66, was seen in September, 1933. The patient had multiple tumors of the skin (Fig. 10). Two months before, one posterior to the right ear had become ulcerated and increased rapidly in size. It had been cut by his barber several months previously and had not healed.

At examination the patient complained primarily of a lesion behind his ear on the neck, which was 3 centimeters in diameter and raised above the skin for about 1.5 centimeters. It was hard, ulcerated and dry (Fig. 12). We noted over the entire body multiple lumps that were in the skin, varying in size from 4 centimeters in diameter down to pinhead dimensions. Some were distinctly pink, and some a little bluish in color. Those deeper in the skin had a bluish cast. The majority of them were on the abdomen and chest, fewer on the legs, especially below the knee. There were some on the feet, and some on the hands, even on the palms. There were none on the scalp.

The tumor on the neck was removed. It proved to be an ulcerated neurofibroma (Fig. 11). The patient did not return until November, 1934. At this time, there was a large stony hard mass in the neck just anterior to the scar. He said that this mass had been present for 6 months and had become larger. He was having difficulty in swallowing food and could take only liquids. He had a constant cough, was greatly emaciated, and in a critical condition. He died shortly thereafter.

One must suspect that the tumor in the neck interfering with swallowing, breathing, and producing a cough, was of neurogenic origin. We are also forced to think that the surgeon who operated did not permit the multiple skin tumors to direct his trend of procedure. It is unfortunate that consent for a postmortem examination could not be obtained.

CASE 5 D.McK., No 24,458, a white woman, aged 25, was seen in November, 1939. When two years old, a small lump had appeared on the lateral side of the right buttock. This increased gradually in size and was removed surgically when the patient was 7 years old. At the same time, the patient had a similar lump on the right buttock which is the beginning of the present large tumor. Following this operation, a number of lumps appeared on the body, first on the left thigh. An attempt was made elsewhere 3 years

go to remove tumor of the right thigh, but the tumor as not completely removed. Pathological report as neurofibroma. It recurred. Since that time, the patient has been able to walk, although she had considerable pain in the right hip in March of this year. This pain had been present for at least a year and one-half and had become worse during the 3 months before she came to the hospital in November 1930. She is unable to walk when first seen.

The details at examination are furnished by Dr. G. W. Kling who is now practicing in Centralia, Washington. The patient was emaciated and lying in bed with the right leg flexed 90 degrees at the hip and abducted 70 degrees. All of the skin was involved by cutaneous and subcutaneous nodules which were extremely soft and easily compressed. They varied in size from match-head to the size of walnut. The skin over the abdomen, legs, arms, and face was pigmented in patches of various sizes. She complained of considerable pain in the right ilium where large tumor mass was present. Apparently this large mass which comprised most of the right side of the abdomen arose from an attempted removal 3 years before of tumor in the right thigh and inguinal region.

The left side of the abdomen, beginning about 6 centimeters to the left of the umbilicus as free of nodules. The entire right side of the abdomen was involved in tumor mass extending deep into the tissues and apparently attached to the right ilium. This mass extended from about 6 centimeters to the left of the umbilicus toward the right around to the sacro-iliac articulation, above, it extended to the costal margin and as limited below by the pubic bones. The surface of this tumor was raised about 6 centimeters above the normal contour and was rough, shiny and red. The large mass consisted of two definite lobes. In the region of the pubic bones, the skin was exceptionally tight, and pain as produced by slight pressure. There was no area of ulceration, but the crevice between the lobes contained small amount of caseous material (Fig. 3).

A small lesion was removed from the left hip for completion of our records. It proved to be neurofibroma (Fig. 14). X-ray of the pelvic bones showed marked involvement of the right ilium (Fig. 5).

This was a typical case of multiple neurofibromatosis in which a neurogenic sarcoma involving bone had developed. It illustrates the disastrous results which accompany ill-informed approach to the surgical removal of a tumor the clinical picture of which was pain. The pediatrician should have definitely in mind the significance of neurofibromatosis so that he can with justification tell the parents that while the disease is usually of no great consequence yet it is apt to progress and may produce hidden symptoms when deeper lesions are associated, also that it can develop malignant changes. Parents or an older child when informed of the characteristics of this condition are prompted to ask, as the years go by for consultations regarding the disease rather than be because they have lived with it peacefully for years, totally unconcerned.

Such an attitude thus created by the pediatrician or general practitioner may be of great profit to the patient as well as to the profession.

The patient is protected and the physician is trained to believe that one or two small lesions in the child might become multiple and therefore diagnostic in the adult. The progressiveness of the disease is emphasized for their attention. They also realize that it may advance to a point of real seriousness. Doubtless, in many instances this stage could often be obviated had the patient been informed.

#### SUMMARY

The clinical significance of a disease is boreed by its frequency. The more people who have it, the more attention it receives. If, on the other hand, a condition is rare, its importance to the physician is reduced in proportion to its rarity. But each discovered instance of it creates definite interest. When a clinical entity seemingly unusual, proves, by reason of its varied characteristics, to be more common than previously thought, its significance increases. But when the disease can be a malignant one, the challenge to us is greater. We as physicians, are obligated to recognize in the benign, the rare possibility of the malignant and to see to it that ignorance on the part of the patient is not our fault. Multiple neurofibromatosis, like leucoplakia, deserves respect as well as watching. Neurogenic sarcoma is best diagnosed prior to biopsy or operation. When associated with neurofibromatosis, a clue is present.

The surgeon deciding to remove a tumor lying in soft tissue must be prepared to do a more radical resection if he finds nerve trunks entering the growth. The close association of neurogenic sarcoma to neurofibromatosis obligates the pediatrician or family physician to warn the parents of a child having that disease of its future possibilities.

The author wishes to express his indebtedness to Dr. Clyde Jensen, pathologist of the King County Hospital for his valuable interpretation of the tissues examined from these patients. The author also wishes to thank Mr. Gertrude Egan for securing the case records and typing the article. He here expresses his appreciation to Mr. Martin Baier, the photographer of the King County Hospital, who is responsible for all the excellent photographs.

#### REFERENCES

1. ADAMS, FRANK E. *Surg. Clin. N. America*, 1933, 357-372.
2. ADAMS, C. W. *Ann. W. J. Schaefer*, 1902, 5: 63.
3. CAMP, A. XII Congress der Ital. Aemti di Pisa, September, 9-15, 1937. *Monatsh. f. prakt. Dermat.*, 1938, 7: 32.
4. CROSSLAND, R. *Glac. Ital. d. med. ven.*, 1907, 26: 11.
5. CHAM, *Surg. Clin. N. America*, October, 1934-1935.
6. EWING, *Neoplastic Diseases*, 3rd ed. p. 167, Philadelphia, W. B. Saunders Co. 1928.

- 7 FEINDEL, E Sur quatre cas de neurofibromatose généralisé Thèse de doct, Paris, 1896, No 104, p 76
- 8 FISCHER, G A Dermat. Wehnsehr, 1927, 84 89
- 9 GARRE, C Beitr z klin Chir, 1892, 9 465
- 10 GERNET, R VON Das plexiforme Librom der Nerven und der Haut. Ein Beitrag zur Geschwulslehre Inaugural Dissertation, Dorpat, April 4, 1892, p 23
- 11 GESCHICKTER, CHARLES Cancer, 1935, 25 377
- 12 GLUGE, G Abhandlungen zur Physiologie und Pathologie, 1841, p 140, cited by Garre
- 13 HEYDWEILLER, E Ein Beitrag zur Casuistik der multiple Fibrobildungen der Haut Inaugural Dissertation, Erlangen, December 30, 1887, p 28
- 14 HOSOI Arch Surg, 1931, 22 258
- 15 JEANSELMIT, L, and ORILLARD Rev de chir, 1894, 14 50
- 16 MACKENZIE, K A J Ann Surg, 1909, 50 295
- 17 PACK, GEORGE T Tumors of the soft somatic tissues in infancy and childhood J Pediat., 1939, 15 372-400
- 18 PENFIELD and YOUNG Arch Neurol Psychiat, 1930, 23 320
- 19 SHOULDS, E Canad M Ass J, 1925, 15 66
- 20 SORGLER, J F Beitrag zur Lehre von den multiplen Neurofibromen Inaugural Dissertation, Erlangen, December 22, 1890, p 31
- 21 STEWART and COPELAND Am J Cancer, 1931, 15 1235
- 22 STOUT, A P Cancer, 1925, 25 1
- 23 THOMSON, ALFRED On Neuroma and Neuro Fibromatosis Edinburgh Turnbull & Speers, 1900
- 24 WESTPHALLEN, H Arch f path Anat, etc, 1888, 114 29

# RADIATION DAMAGE TO TISSUE AND ITS REPAIR

ERNEST M. DALAND M.D. F.A.C.S. Boston, Massachusetts

THE roentgen-ray is a powerful physical agent. When it was first discovered its action was not well understood, and the dangers connected with its use were not realized. Much damage resulted, both to the physicians and technicians using it and to the patients. Its use at that time resulted in few cancer cures. Later as its action became better understood and new measures were introduced for the protection of workers and patients, the damage resulting was reduced to a minimum. In this second era the greatest number of cures were of skin cancers. In many other types of cancer the roentgen-ray seemed at first to retard the growth but the results were not lasting. In other words, it almost cured cancer.

With the development of higher voltages and the use of larger dosages over long periods of time, we have all observed a striking improvement in the results. Now we see many cures in patients who a decade ago would not have been helped. However we repeat that we are dealing with a powerful agent which may do great damage to normal tissues as well as to abnormal tissues. Radiologists are well aware of these dangers and rightfully expect assistance from the surgeons. Unless surgeons are able to repair damage from radiation, roentgenologists will not use intensive doses and they will not cure as many patients.

There was a time when many radiologists were afraid to cause erythemas or ulcerations of the skin for fear that the patient would accuse them of having "burned" him. If the situation is explained to the patient and, if he knows that his skin is going to get red and sore, there will be few legal complications.

In considering radiation damage to tissue we must distinguish between temporary and permanent changes. We must consider the early injuries and the late damage. We wish to know the degree of damage, whether the tissues are ulcerated superficially or deeply edematous, fibrosed, or whether there is actual necrosis. Finally we are interested in the late degenerative changes in the tissues and in the development of cancer in certain instances.

The mildest form of radiation damage is the erythema or blush on the skin. All x-ray machines are calibrated as to the amount of irradiation necessary to give an erythema. Usually several times this erythema dose is used to destroy a lesion. A simple erythema may be followed by desquamation, a severe erythema by ulceration. Often the radiologist treating cancer produces an ulceration and thereby feels that he has delivered the maximum dosage possible. These reactions in the skin are accelerated, delayed, or prolonged according to the amount of treatment given daily and the total number of treatments. Modern technique is based on the fact that if the treatments are carried out over a period of from 3 to 4 weeks the treatments are more effective on the neoplastic tissue and the damage to normal tissues is lessened. Ordinarily the ulcerations of this type are ugly in appearance but give little pain and usually heal within a few weeks. If the patient is told what to expect he will have few complaints.

As much treatment as is necessary should be given during the first cycle before permanent changes appear in the tissues. Later the skin becomes thickened, edematous, and leathery the blood vessels become narrowed and carry a decreased supply and there is fibrosis of fat and subcutaneous structures. Once these changes have set in, further treatment must be given with caution. The effect on the tumor will never be as great in a second series as in the first and the amount of damage to tissues already fibrosed will be greater. Painful, persistent ulceration may appear and this will require surgical measures to remedy it.

Infection entering an area previously heavily irradiated may cause extensive necrosis and sloughing of the area. Lesions in the mouth, pharynx, rectum, and bladder are particularly susceptible to infection after irradiation the skin is not as fertile a field for infection.

Ischemia of tissues is the forerunner of necrosis. Patients with arteriosclerosis and the resulting endarteritis, syphilis, and diabetes may have such circulation that

circulation that  severe irradiation

a dissection of the glands of the neck or a radical amputation of a breast may interfere with the circulation of those flaps. The extra burden imposed by roentgen therapy may be sufficient to cause death of the skin flaps.

Whenever irradiation is given through normal skin to an underlying cancer and the treatment is given in sufficient doses to destroy cancer, the normal skin and any other normal tissues in the path of the rays will receive permanent damage. This is an argument used by some for not giving "prophylactic treatment" after an operation for a condition which appears to be favorable. However, this fact should not be used to halt necessary treatment, for these damaged tissues can be repaired if late changes occur.

Irradiation reaction during the first few months after treatment consists in bronzing of the skin, endarteritis, and fibrosis of the subcutaneous tissues. This may not be severe enough to cause serious damage. However, if a large artery supplying this damaged area is ligated, complete necrosis of the entire irradiated field may develop within a few days. We have seen the same type of necrosis after an alcohol injection of the mandibular nerve for relief of pain.

Late changes in an irradiated field comprise telangiectases of the skin, followed by hyperkeratoses in the skin, alopecia, fissures, fibrosis of and later loss of the subcutaneous fat, marked endarteritis of the smaller vessels, and degenerative changes in the fascia. The extent of these late changes depends on the amount of irradiation originally given, the time interval and the region involved.

The most serious of all complications from irradiation is the development of cancer of the skin in the treated area. Ewing points out that there is an incubation time between the use of roentgen-rays and the development of cancer of from 3 to 11 years. The shortest incubation time we have seen is  $2\frac{1}{2}$  years and the longest 18 years. Roentgen cancer is usually of the epidermoid type. It is slow to metastasize but when it does, metastasis is rapid and extends at first in the lymphatics and finally in the blood stream.

The scope of this subject is so great that many types of injury can be barely mentioned and others not considered at all. All irradiation therapy is based on the theory that malignant cells are susceptible to doses that will not seriously damage the normal cells. That presupposes that we know exact extent of lesion to be treated which, of course, is not always true. Unfortunately, the depth of the treatment cannot be entirely controlled.

The mucous membranes of neighboring organs may be nearly as susceptible to the roentgen-ray

as the tumor itself. It has been demonstrated by Warren and Spencer that permanent damage to the lungs may follow therapy to the breasts and chest wall. It is well known that irradiation of the uterus may produce ulcerations in the rectum and bladder as well as fistulas, and that intensive therapy over the intestines may cause ulceration. We have seen one pathological fracture of the femoral neck due to roentgen therapy of the inguinal nodes.

#### TREATMENT

Treatment of these injuries cannot be described in a paragraph. No two tumors offer the same problem, no two cases of irradiation damage can be handled in the same way. In general, it may be stated that treatment will be based on removal of tissues which are damaged beyond their own power of repair, on the relief from infection, on short-circuits to avoid continual irritation of an involved organ and in the replacement of tissues by free grafts or flaps. Treatment may be prolonged, but the relief afforded is so satisfactory to the patient that time is a small factor.

We have collected a group of cases illustrating the types of injury which we are meeting, and we have described the methods of repair used. These cases illustrate all degrees of permanent damage and include several which have shown late malignant changes.

*Group I. The removal of superfluous hair by roentgen therapy.* A decade ago it was common practice for certain beauty parlors to advertise the removal of superfluous hair by the "Tricho system." This treatment proved to be x-ray treatment, apparently given without adequate control of dosage. Four cases are cited, in 2 painful necrosis occurred and in 2 malignancy developed. It is probable that, if given enough time, cancer would have appeared in all these lesions.

CASE 1. H. S., age 49, was seen on October 31, 1939. Fourteen years before he stated that he received x-ray treatment by the "Tricho" system for superfluous hair on both upper arms and shoulders. The hair disappeared and he had no trouble until 4 years before when, following a sunburn, the lesions began to itch very badly. He had been under observation by a dermatologist since then and there had been no suspicious areas until this examination.

Examination showed an area of irradiation dermatitis extending from just above the tip of the shoulder nearly to the elbow and covering a full half the circumference of the arm. In the center the tissue was very hard and in places nodular. Around the borders the skin was soft but showed marked telangiectases. It was felt that the nodular areas might be beginning malignancies and treatment by excision and graft was advised. The other arm showed the same condition without the induration (Fig. 1).

Operation was done on November 7, 1939, at the Baker Memorial Hospital. The area of dermatitis was excised. The subcutaneous fat was extremely indurated and it was



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From the Needville Hospital and Cancer Section, Westfield Massachusetts (Massachusetts Department of Public Health) and the Massachusetts General Hospital.

Presented in the Symposium on Cancer, before the Clinical Congress of the American College of Surgeons, Chicago, October 7-15, 1940.

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Infection entering an area previously heavily irradiated may cause extensive necrosis and sloughing of the area. Lesions in the mouth, pharynx, rectum, and bladder are particularly susceptible to infection after irradiation: the skin is not as fertile a field for infection.

Ischemia of tissues is the forerunner of necrosis. Patients with arteriosclerosis and the resulting endarteritis, syphilis, and diabetes may have such poor circulation that they tolerate irradiation poorly particularly in an extremity. Irradiation of cancer in the tongue of a syphilitic is not so satisfactory for undue sloughing appears.

Irradiation over an operative wound must be carried out cautiously. The elevation of flaps is

up of the epithelium in the form of hyperkeratoses and numerous pinpoint ulcers. On the other leg there were numerous keratotic areas.

The first operation was done at the Phillips House on July 14, 1934. An area  $3\frac{1}{4}$  by  $1\frac{1}{2}$  inches wide was excised and a secondary graft done. Microscopical examination showed radiation dermatitis but no malignancy.

During the past 6 years numerous other areas on both legs, sometimes several square inches, have been excised and grafted. The circulation at the base of these ulcers has been very deficient and fat has been entirely absent. None of the specimens has shown malignancy. With the exception of a small malignant lesion on his nose he has not developed radiation dermatitis or necrosis anywhere except on the lower extremities. He is an extremely active individual on his feet. His dorsalis pedis arteries are palpable. Probably his activity has aided his circulation and has prevented extreme necrosis and gangrene of his extremities.

*Group III Roentgen therapy of lesions on the extremities.* Case 7 cited above, could well be included also in this group. It is apparent from that case and those which follow that the same amount of therapy that would be used on the face, neck, or trunk cannot be used safely on the extremities.

CASE 8 M. S., Westfield Sanatorium 1145, age 65, was admitted on February 8, 1939, with a large ulcerated growth on the dorsum of the left wrist. The duration was 4 years and he had received no treatment. Examination showed an ulcerated lesion extending across the entire dorsum and lateral aspects of the wrist, measuring 9 by 7 centimeters. There was good motion of the fingers, but the wrist was fixed with 40 degrees dorsiflexion. The examining physicians stated that he would probably require amputation, but felt that roentgen therapy should be tried. Biopsy showed necrotic cancer.

During the next month he received 6000 r at 200 kilovolts through an 8 by 10 centimeter portal, directed to the dorsum of the hand, and 2100 r to the medial and lateral aspects of the hand, 400 r at a treatment. There was marked regression of the cancer but the ulcer became deeper, necrotic, and foul. Pain was not a great factor. Ten weeks later there was no healing, but no cancer could be seen (Fig. 7). Amputation was done at the junction of the upper and middle thirds of the forearm. The pathologist could find no cancer in the specimen submitted but there was marked irradiation reaction.

This is an example of roentgen therapy given to a region with poor blood supply and little subcutaneous fat in an elderly man. The dosage was adequate to destroy the cancer, but regeneration could not be expected to occur on a tendon sheath base, particularly in the face of extensive infection and necrosis. Amputation in such cases is the only satisfactory method of treatment.

CASE 9 S. A., age 58, was first seen in 1924. She gave a story which dated back 20 years, having begun with a swollen gland in the neck which broke down and formed sinuses. She then had sinuses in the bones of her right wrist and jaw and later further sinuses over her ankles and bones of the lower leg. She was treated 20 years previous to examination by x-ray and again 13 years previously. She also had lupus on the face treated by x-ray. Apparently she had multiple manifestations of tuberculosis in the skin, bones, and glands.

At the time of the first examination she had extensive carcinoma on her nose. The entire nose was removed. Later she developed a carcinoma on the right side of the face in an area formerly treated by x-ray for lupus. The lesion on the right cheek was excised and closed with a large full thickness graft. There was no recurrence of these areas after they were operated on. In 1935 she developed carcinoma of the left breast. Radical operation was done and the pathological report was colloid carcinoma without metastases. In 1937 she developed carcinoma of the right breast. Radical operation was done, and this was reported as grade 3 with axillary involvement. At this time she called my attention to a growth on the right leg in an area of x-ray dermatitis. This was excised and found to be carcinoma. Again in May, 1940, she appeared with another growth on the opposite leg. This was around a chronic sinus and this time the pathology was both tuberculosis in the sinus and carcinoma in the skin around it. At the present time she has metastases in her spine from the second carcinoma of the breast.

In this case her facial cancers occurred in old lupus scars. Even though she received roentgen therapy it is uncertain whether the therapy or the tuberculosis was the activating agent. It is striking that, next to her face the areas on the extremities should have been the first to break down.

CASE 10 A. P., age 47, was admitted to the Pondville Hospital in May, 1938, with multiple basal cell carcinomas of the temple, back, and right ankle. Approximately the same dosage of roentgen therapy (high voltage) was given to each area and additional treatment a month later. All lesions healed and have remained healed until recently when the area above the right ankle became tender and broke down (Fig. 8). After 2 weeks he sought relief from his pain and the area was excised. Microscopical examination showed irradiation necrosis. This necrosis occurred 18 months after his last treatment.

#### *Group IV Injuries to roentgenologists and other workers in roentgenology*

CASE 11 J. B., age 60, roentgenologist, was first seen in April, 1939 complaining of ulceration of the middle phalanx of the left index finger. For many years he had noted an increasing amount of dermatitis of his hands but the present lesion had come on rather suddenly. The left forefinger and middle finger showed very marked telangiectases particularly on the dorsum. The nail was corrugated and beneath it was a large area of hyperkeratosis. The nail was exceedingly tender. At the base of the nail, close to the inner phalangeal joint, was an area of ulceration (Fig. 9). The pain in this was severe enough to require opiates.

He was operated on at the Baker Memorial Hospital on May 2, 1939 and the involved area of skin on both the forefinger and middle finger was removed. The defects were covered with Thiersch grafts. The ulcer was found to extend deep down toward the joint and to have destroyed the tendon attached to the terminal phalanx. As a result, he had some permanent flexion of the terminal phalanx, and the tissues about the nail were extremely atrophied. Later amputation of the terminal phalanx was done on this hand.

The pathological report on area excised and on amputated phalanx was "irradiation necrosis with no malignancy."

CASE 12 H. P., a 26 year old physician was examined on October 30, 1935. Fifteen months before he burned the fingers and thumbs of each hand while setting a fracture under the fluoroscope. It is said that this procedure re-

necessary to remove it down to the muscle. The defect was covered by several Thiersch grafts. The pathological report stated that irradiation dermatitis as present but no malignancy. "The microscopic sections show diffuse dermatitis with slight keratinization of the epidermis, flattening of the papillae, and dense acellular avascular fibrosis of the corium in which no hair follicles or sweat glands are noted. There is moderate lymphocytic infiltration throughout and one section shows a localized superficial area of edema resembling tiny bulla. A polymorphous-clear leucocytes and narrowing of the epidermis in this region. The arterioles show slight subintimal proliferation."

CASE 2. E. G. Wentfield (Sussexton No. 2,649, age 30, was admitted April 7, 1940. She states that she received x-ray treatment by the "Tricho" system about 9 years ago for superfluous hair. One year ago she noticed an ulcerated area near the angle of the mandible. This has increased in size and a recent biopsy showed epidermoid carcinoma, grade . On examination both cheeks and upper cervical regions showed generalized skin atrophy with telangiectases. In the center of the irradiated area on the left, as an ulcer 2.5 by 8 centimeters which was obviously malignant (Fig. 3).

Surgical excision of the ulcer and part of the trophic area was done and reported to be epidermoid carcinoma. She made good recovery. It will be necessary to excise all the irradiated tissue in this patient as she will undoubtedly develop new malignant areas.

CASE 3. F. L., age 38, was seen in March, 1937. Several years before she had received x-ray treatment at London, for hair on her chin. A dermatitis developed and finally an ulcer on the chin. Examination showed marked telangiectases with ulceration and induration around the ulcer suggesting malignancy. Excision was done at the Beth Israel Hospital in March, 1937. The entire area of dermatitis was removed and segment of the mandible was chipped off. Later the defect was closed with Thiersch graft. Unfortunately the apophysis was lost and there was no microscopic examination but the gross appearance was that of cancer. At the time of operation no subcutaneous fat was found and none appeared to form beneath the graft following operation. She was followed for number of years after operation and was very much dissatisfied with the appearance of the graft. The graft remained extremely white (Fig. 3) and she had great difficulty in using cosmetics to make her presentable. On several occasions the matter of removal of the graft and closure by flaps was suggested but as she had other surgical conditions which were more urgent this was postponed. It was later done, however by another surgeon.

CASE 4. V. S., age 48, teacher, as seen on September 6, 1938. In 1935 she had received x-ray treatment by the "Tricho" system for superfluous hair on the legs. Three years later she noticed changes in the skin and these increased year by year. During the past year dermatologist had given her 4 radium treatments without benefit to the affected area.

Examination showed grayish, painful ulcer 4 by 3 centimeters over the calf of the right leg. The edges of the ulcer were raised and firm. Around the ulcer the skin showed telangiectases, induration, and loss of subcutaneous fat. There were no palpable regional lymph nodes. A diagnosis of x-ray dermatitis with possible malignant change was made (Fig. 4). Operation and graft are advised.

Operation was done at the Baker Memorial Hospital on September 9, 1938. All the involved skin was excised and the deep fascia was removed. An immediate Thiersch graft was done. Pathological studies showed acute inflammation with necrosis, but no cancer was found. Areas of necrosis appeared in the graft but healing took place rapidly.

The characteristic features of these lesions are telangiectases of the skin, dryness with itching, poor blood supply and either changes in, or loss of the subcutaneous fat. The treatment is always removal of the affected skin down to normal tissue. Radiation treatment for this condition, as was done in Case 4, should be condemned.

Group II. Roentgen therapy for dermatological lesions with late degenerative changes. The following cases are illustrative of this group.

CASE 5. M. M., age 68, was examined on June 8, 1934. She had had psoriasis for years, one on the knees and elbows. T and one-half years previously she received x-ray treatments over the knees and over the elbows at set intervals. Five days after the last treatment the knees became black, swollen, and painful. The elbows were the same to lesser degree. She had to go to bed because of pain and stayed there 7 months. The treated area became raw and discharged constantly. Her doctor treated her with boric acid and electrolysis, but this made her worse. She went to another doctor who treated her with special serum he obtained in Chicago. She had injections of this at \$45.00 treatment with no benefit.

Examination revealed that both elbows and right groin had extensive radiation changes in the skin but no ulceration. Both knees showed similar radiation changes with central deep ulceration 3 inches across. The left elbow showed area of new growth (Fig. 5). Excision with skin grafts was advised.

Operations were done at the Baker Memorial Hospital on June and July 5, 1934. The areas of dermatitis over both knees were excised at the first operation. Thiersch grafts are applied to the granulating wounds at the second operation. Lesion over left elbow was excised and defect covered with full thickness graft. Recovery was satisfactory. Microscopic examination shows x-ray burns with areas of carcinoma over the left knee.

CASE 6. F. D., age 26, colored male, Massachusetts General Hospital 836, as first seen on March 24, 1939. At 5 years of age he had received, in another hospital, x-ray treatment to his entire scalp for ringworm. The hair failed to grow on the right side. One year before entrance he noticed small scaling area in the center of the bare area. This gradually increased in size. At times the crust came off, and there was profuse and persistent bleeding.

Examination showed an area of alopecia over the right temporoparietal region. In the center was raised area 34 by 34 centimeters with moderate induration. There was loss of pigment in much of the area (Fig. 6). Malignancy is an irradiated area, suspected and excision is done of the portion showing the most marked changes. Microscopic examination showed deep fibrosis. No "verruca" in the center. The area was covered with graft which was not entirely satisfactory but healing eventually occurred.

CASE 7. I. H., age 50, was examined in July 1934. complaining of ulcers on his legs. For many years he had suffered from eczema involving the whole body. He had tried every known remedy without relief. Seven years before he had received x-ray treatment to various parts of the body but chiefly to his legs. Ten years previously he began to develop an irradiation dermatitis on top of his eczema. One malignant ulcer had been excised.

Examination showed an extensively exfoliating eczema of the whole body. On the inner aspect of the right lower leg there was an area of skin with poor circulation. The skin was dry showed numerous telangiectases, some heaping

platinum needles. He later received irradiation to several hard lymph nodes in the right side of the neck.

One week after this treatment was completed he was readmitted because of severe hemorrhage from his tongue. The external carotid artery was ligated and the bleeding was checked. He was followed in the clinic. One month later a severe radiation reaction in the skin and mucous membrane of the mouth was noted. There was marked edema of the face and he was unable to open his mouth. Three weeks later he was again admitted.

He was in a critical condition. The edema of the face had increased. There was an area of gangrene of the entire field treated by x-ray. On removal of the gangrenous tissue extensive ulceration of the side of the tongue, the alveolus and floor of the mouth, was noted. Death followed in 5 days. No autopsy was performed.

CASE 18. A. C., age 50, was seen at the Massachusetts General Hospital in August, 1937 with a carcinoma of the buccal mucosa. He received high voltage therapy externally over a period of 1 month. After these treatments had been started he went to his dentist and had some teeth extracted. Two months later he had a severe hemorrhage from the cheek and had an emergency ligation of the external carotid artery. Within a few days there was evidence of circulatory change and he was referred to the Pondville Hospital December 20, 1937. There was marked edema with swelling of all the area which had been irradiated. Rapid changes occurred in the irradiated area and all the treated tissues became gangrenous and were removed. In spite of the large amount of therapy which he had received a recurrence developed along the jaw and extended to the tonsil. Death occurred within a few weeks.

*Group VIII. Repeated roentgen therapy for plantar warts.* We have recently seen a group of patients suffering from irradiation necrosis of the sole of the foot. In each case treatment had been given with relief at first. However, when treatment was given for a recurrence of the wart necrosis followed.

CASE 19. T. M., age 21, was seen on October 30, 1939. Four years previously he had received x-ray treatment for plantar warts. Several treatments were given at weekly intervals but the type of treatment and the dosage are not



Fig 1. Case 1. Irradiation dermatitis following roentgen treatment for superfluous hair. No malignancy.

known. Three years later the warts recurred and he received treatment in November, 1938, February, 1939, and in May, 1939. High voltage therapy at a distance of 20 centimeters was used.

Following treatment the warts cleared up and he spent his summer in active athletics, much of the time wearing sneakers. He knows of no direct trauma but in August a painful ulcer appeared and for 4 weeks he has been confined to a hospital and has required opiates to relieve his pain.

On November 4 he was operated on at the Baker Memorial Hospital. The lesion was excised down to normal fat. A pedicle graft was lifted from the opposite thigh and sutured in place on the foot. A plaster spica including both legs was applied and this was left in place for 2 weeks. At the end of this interval the flap was divided and sutured in place on the foot. Weight bearing was started 3 weeks later and he walked normally 2 months after removal of the ulcer. There has been no recurrence of the ulcer.

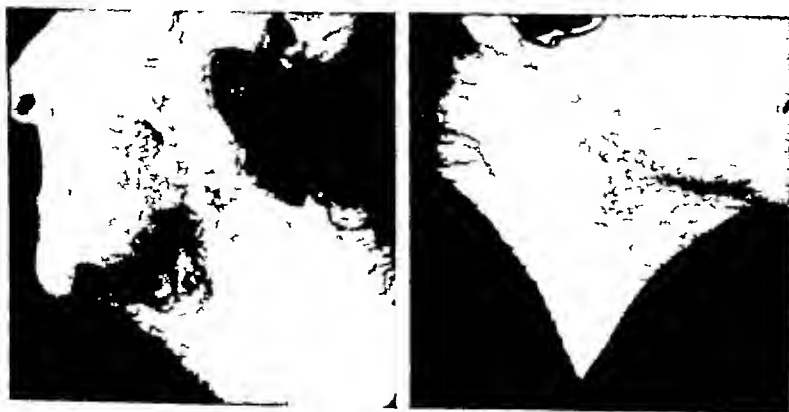


Fig 2. Case 2. Irradiation dermatitis following roentgen therapy for superfluous hair. Carcinoma is present on the left side of face.

quired one and one-half hours. A marked reaction appeared within a week, followed by ulceration and severe pain in the right index finger. The ulcer was removed and flap applied from the chest. Healing occurred in 6 months. He had previously developed a painful ulcer in the left index finger. Examination showed gangrenous, acutely tender area covering the terminal phalanx and half of the middle phalanx of the left index finger. Partial amputation, as advised and done by another surgeon. Six weeks later he again appeared with a new acutely painful ulcer at the tip of the middle finger on the left hand (Fig. 3). There was also an area of dermatitis and atrophy on the thumb. He was advised to enter the hospital the following day which he did. In the interim the skin of the thumb broke down and painful ulcer developed in a few hours.

Operation as done at the Baker Memorial Hospital on December 6, 1935. All the damaged skin on the left thumb and middle finger was excised and the defects closed with full thickness skin graft. In February a new ulcer appeared on the right middle finger and the irradiated area was excised and grafted. All grafts took quite well and he has remained free from further trouble (Fig. 4 and 5).

CASE 3. E. F. age 70, former X-ray technician and photographer as seen in August, 1927. He had done great deal of work with X-ray during the early years of its development and had sustained extreme chronic burns of his hands. He had been treated in numerous hospitals and had many operations. On examination he showed loss of his forefinger and little finger on the right hand (Fig. 6). The ring finger was involved in large cauliflower mass which extended down into the palm. The function of the thumb and middle finger was fair. On the other hand he had lost his fingers. Operation was carried out at the Massachusetts General Hospital in August, 1929. The ring finger and corresponding metacarpal were removed together with the growth. A skin graft was applied over the defect (Fig. 6). There has been no recurrence. During the past year he has been able to do good deal of careful work as photographer and cabinet maker. His thumb and finger on one hand and thumb and two fingers on the other.

#### Group V Ulceration of an abdominal scar with fecal fistulas

CASE 14. W. J. age 50, was first seen in 1910. A few months before he had noticed mass in the left lower abdominal quadrant. He was traveling in Texas at the time and an exploratory laparotomy was done. A large retroperitoneal tumor was found and it was thought to be sarcoma. A biopsy was done. A course of X-ray treatment was given following operation.

He came to Boston few months later and had second series of treatments. This time deep therapy was given at the Huntington Hospital through the anterior and posterior portals. Six months later he received further treatment through lateral portals. A few weeks later his abdominal wound broke open and he developed several fecal fistulas. He was operated on by the late Dr. R. B. Greenough and an anastomosis was done between the cecum and rectosigmoid. He continued draining through fistula in the scall late in time, however. A few months later he began to discharge large quantities of hair and pieces of jaw bone from his wound. This, of course, made the diagnosis one of dermoid cyst rather than one of malignancy. Gradually the entire abdominal wall broke down and he had numerous operations and closures of fistulas. Finally one small fistula remained together with the fistula into his dermoid cyst. About this time he developed pernicious anemia. As he happened to be under treatment at the Huntington Hos-

pital at that time he came in charge of Dr. George Howe and his associates and he responded well to liver therapy. Due to the destruction of the abdominal wall and the abdominal muscles his abdomen was very much contracted and he altered in bent over attitude and it was not possible for him to walk. He gradually improved but in 1926 he developed metastatic carcinoma in the cervical lymph nodes. Later he was found to have carcinoma of the posterior wall of the pharynx, and he died from this condition.

This patient was treated in the early days of deep therapy and while he did not have an amount that we would consider excessive today he did have more than his recently healed abdominal wound would stand. Infection from that ruptured wound destroyed much of the irradiated tissue over the rest of the abdomen.

#### Group VI Necrosis of bone and cartilage.

CASE 5. K., age 63, was first seen at the Providence Hospital on January 9, 1935, with an extensive carcinoma involving the left lower jaw and extending back to the anterior pillar and its radiation extending into the sub-mandibular region. Roentgen examination showed bone destruction. The patient's mouth was fairly clean, and he was edentulous. Gold seeds of radon were inserted into the tumor and deep therapy was given externally. There was good response to the treatment. Three months later his bone was visible, and he had a large opening in his cheek.

For the next 7 years the necrotic bone continued to come away. The bone was resampled many times and numerous attempts were made to close the fistula. There was never any reappearance of the cancer. In May 1935, the fistula was closed successfully and the last bit of exposed bone came away. He died without recurrence in 1938 at the age of 73 years.

Irradiated bone is "stink" bone, but it is not dead. There is no tendency to sequestration and there is no line of demarcation. We have successfully sequestered irradiated bone on several occasions and have produced heat necrosis with later sequestration.

CASE 6. A. B. age 50, was first seen in the cancer clinic of the Westfield Massachusetts on June 5, 1935, with a basal and squamous carcinoma of the bridge of the nose, of 4 years' duration. He was given one treatment of high voltage therapy. The lesion had completely healed in 6 weeks, but there was edema and redness of the septum. Fourteen months later he complained of increasing pain in his septum and shortly after perforation appeared with relief of his pain. This definite destruction of cartilage occurred 10 months after therapy.

Group VII Ligation of vessels supplying an irradiated area. In case of hemorrhage, ligation of the vessel supplying the part is often done. If this region has previously been subjected to roentgen damage, such a ligation may deprive the tissues of all their nourishment and gangrene may follow.

CASE 7. B. M., age 61, Providence Hospital No. 4391, was admitted on January 27, 1934, with an ulcerated, indurated lesion on the right side of his tongue. This was treated by electrosurgical excision and the implantation of

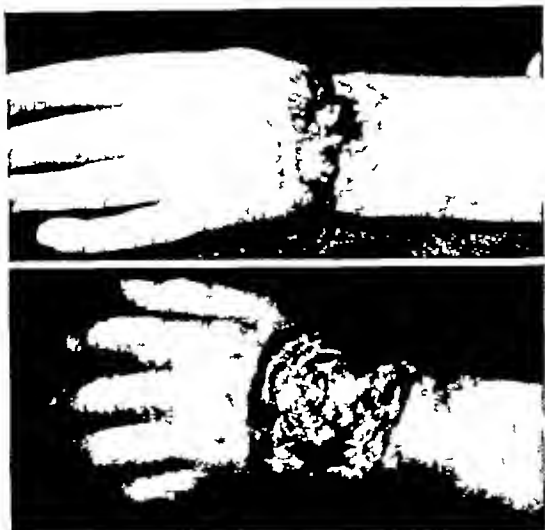


Fig 7 Case 8 Above, carcinoma of dorsum of hand before treatment. Note that fingers are essentially normal. Below, after roentgen therapy. The carcinoma has been destroyed, but there is deep necrosis. Note the useless fingers. Amputation was done.

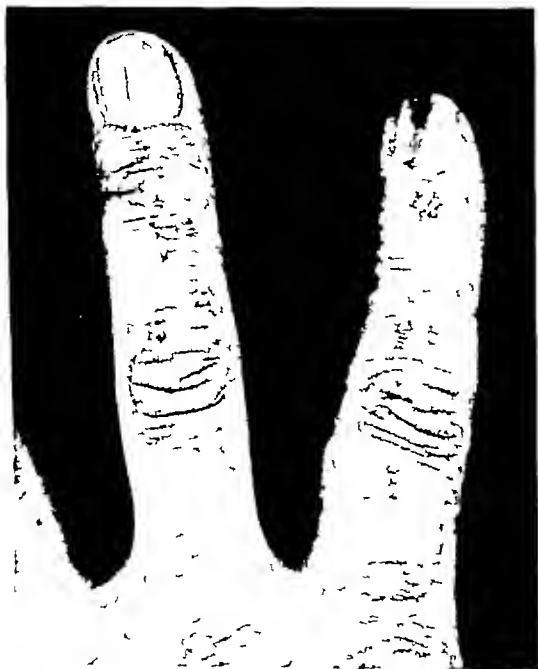


Fig 9 Case 11 Late irradiation changes in the fingers of a roentgenologist. Note the fissured nails, loss of pigment, the subungual hyperkeratosis and the ulcer at the base of the distal phalanx of the forefinger.



Fig 8 Case 10 Late necrosis of skin above ankle 18 months after high voltage roentgen therapy.

had been no biopsy in the apparent recurrence. Complete x ray examination of the bony skeleton was made and no metastases were found.

Operation was performed at the Baker Memorial Hospital on October 14, 1938. The entire area of dermatitis was excised down to the ribs and intercostal muscles. A flap 7 by 4 inches was dissected up from the abdominal wall and rotated to fill the greater part of the defect (Fig 13, b). A second flap was dissected from the lower abdomen to fill the second defect. A small part of the flap sloughed and a skin graft was done 2 months later. The pathological findings were x ray necrosis and inflammation but no tumor. She developed necrosis of one rib, and this gradually sequestered. She had received complete relief from her chest pain and was able to be quite active again. However, about 6 months after the lesion was excised she began to show evidence of bone metastases. These developed rapidly and she died in September, 1939, with metastases in



Fig 10 Case 12 Partial amputation of left index finger after an acute x ray burn. Note also ulcer of tip of middle finger and area of irradiation dermatitis on thumb.



Fig. 3. Case 3. An area of irradiation dermatitis and probable carcinoma, as excised 5 years before. End-result of Thiersch graft. Note the extreme whiteness of graft.



Fig. 4. Case 4. Left, Irradiation necrosis after roentgen therapy for suppurative boil. Appearance of Thiersch grafts 1st dressing after operation.

*Group IV. Painful ulcers follow successful eradication of cancer by roentgen therapy*

CASE 20. O. N. gr 45, as seen in June 1938, with painful ulcer on the chest wall. Ten years before, the right breast had been removed for several solitary tumors. The pathologist reported that these were benign. However 3 years later red nodule appeared in the scar. This gradually changed in size and appearance and 2 years ago she received ray treatments in neighboring state. Following her treatment she developed reaction which took 4 months to heal. It remained healed for 1 year and 8 months ago it began to break open. It has gradually spread until the entire irradiated area has become involved (Fig. 5.)

Relief of pain, as the problem in this case. It is not felt that the original lesion had been malignant and there



Fig. 5. Case 5. Irradiation necrosis after roentgen therapy for parietals Carcinoma, as present on the left.



Fig. 6. Case 6. Lat. Irradiation necrosis after roentgen therapy for ringworm of the scalp

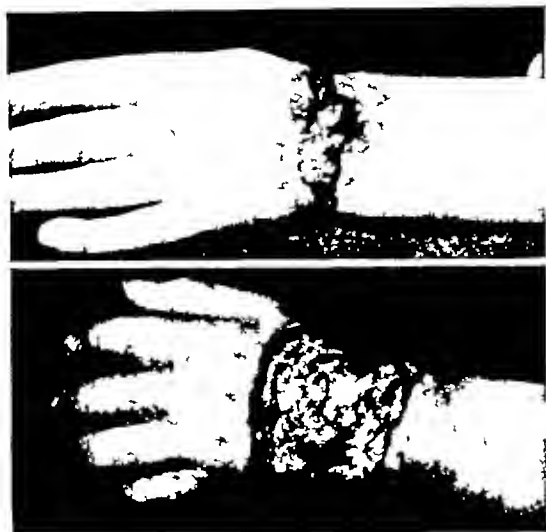


Fig 7 Case 8 Above, carcinoma of dorsum of hand before treatment Note that fingers are essentially normal Below after roentgen therapy The carcinoma has been destroyed, but there is deep necrosis Note the useless fingers Amputation was done



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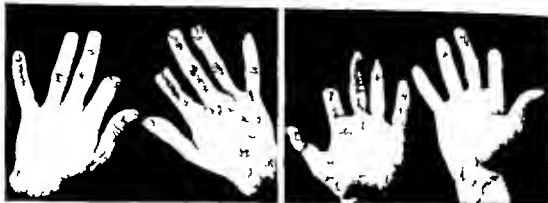


Fig. 1. Case 1. a, Note amputated terminal phalanges of each forefinger and irradiation dermatitis of thumbs and middle fingers. b, After excision of areas of irradiation

dermatitis and application of full thickness grafts. Note the poor result of treatment of the middle finger. It has complete loss of fat and the prominence of the phalanx.

right humerus, right scapula, left femur and spine. She also developed extensive disease beneath pectoral muscles.

The ulceration in this case was caused by the legitimate attempt at destruction of her tumor. This was accomplished. Surgical treatment was attempted with the hope of permanent cure but proved to be only palliative treatment, because of the development of extensive metastases.

CASE 3. J. K., Westfield Sanatorium No. 356, age 58, admitted June 7, 1930, with raised, ulcerated lesion 4 by 5 centimeters over the sternum. This had been present for about 20 years and biopsy examination showed basal cell carcinoma. Definite fixation to the sternum made it appear inoperable. However roentgenograms did not show invasion of the sternum (Fig. 4, a).

He was given 5000 R with the 200 Libby machine delivered through a 33 centimeter cone over a period of 7 days, ending July 2, 1930. There was immediate regression of the tumor. There was no sign of healing. Bone necrosis followed and deep infection of the chest wall required drainage. A large piece of sternum has come away but there is still a large area of radiation osteitis (Fig. 4, b).

The writer was asked to operate on this patient, but felt that roentgen therapy was better. Looking back, we now feel that excision with coagulation of the involved pericosteum would have been a better method of treatment.

Group V. Roentgen therapy: lumbosacral region. During the past 2 years we have followed

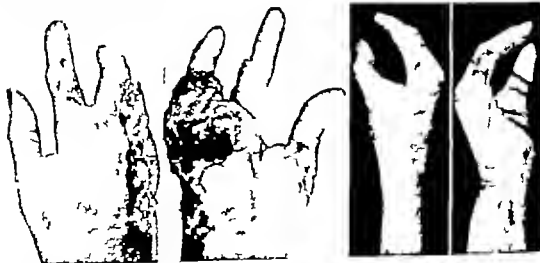


Fig. 2. Case 3. a, Late results of roentgen damage to an early worker with development of cancer in damaged areas. Note the absence of the fingers. b, Right, 6 months

after excision of the cancer and application of Thiersch graft, finger and thumb are very useful. Numerous areas of hyperkeratosis on the finger and thumb.



Fig 13 Case 20 a, left, Recurrent carcinoma of breast following extensive roentgen therapy. The entire irradiated area is ulcerated and very painful. b, The ulcer has

been excised and closed by means of a flap from the abdomen. A necrotic rib is shown. Patient has been relieved of all her pain.

4 patients who have developed radiation necrosis of the lumbosacral region. This appears to be a site particularly likely to be damaged by large doses of roentgen therapy. In the following case radiation necrosis occurred in this region and also on the anterior abdominal wall.

CASE 22. T. S., age 59, a retired school teacher, was seen in November, 1938, and admitted to the Baker Memorial Hospital. A tumor of the intestines had been removed in 1926, but no microscopic examination was made. In 1930 a second operation revealed "a very extensive carcinoma with involvement of all the retroperitoneal glands and liver" but nothing was removed for examination.

From 1930 to 1932 she received x-ray therapy (type and amount unknown) through anterior and posterior portals. In 1934 she developed induration about the umbilicus. This was excised but the wound never healed. Later she

developed an ulceration over the sacrum. In the meantime she had noticed enlarged axillary and cervical nodes and as these responded to small doses of x-ray it was thought probable that these nodes as well as the abdominal nodes represented lymphoma. The ulcer of the abdominal wall had been present for 4 years and had troubled her chiefly because of the odor. The posterior ulcer, present for 3 years, gave constant pain.

Examination showed absence of the umbilicus. Surrounding its normal position was an extensive area of irradiation dermatitis with telangiectasias around the periphery and a deep ulcer extending down to the fascia (Fig 15, a). There was a similar ulcer with less depth over the upper portion of the sacrum (Fig 15, b). Operation was advised.

On December 6, 1938, operation was performed on the posterior ulcer. An incision was made around the periphery of the irradiated tissue through normal skin. The wound edges were beveled in to the edge of the normal fat which

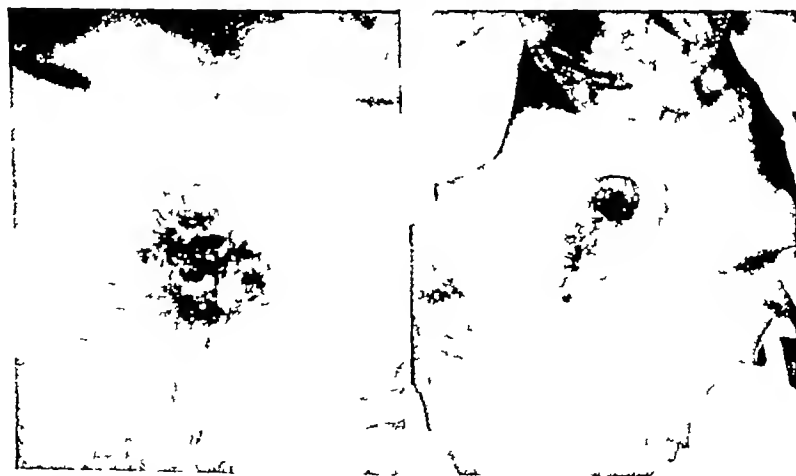


Fig 14 Case 21 a, left, Basal cell carcinoma overlying sternum. b, The same lesion following deep therapy. The sternum is necrotic. An abscess around the lesion has been drained on the right.



Fig. 5. Case 2. a, left, Irradiation dermatitis and necrosis of anterior abdominal wall about umbilicus. The necrosis extended to the peritoneum. Lesion excised and closed by flap from below. b, Same patient, showing similar area over sacrum. Lesion excised and closed by flaps from buttocks.

as entirely absent around the ulcer. One layer of fascia was removed. This left a layer of fascia overlying the muscles. Numerous incisions were made in this fascia to aid the formation of granulations. The fascia had a peculiar gray appearance and did not look healthy.

Two months later there was very little evidence of healing. The wound was covered with gray hyaline like serum which could be separated with scissors but which reappeared in 2 or 3 days. At the time of operation on the anterior wound this surface was again curetted and another layer of necrotic fascia removed down to the sacrospinous group of muscles. Dakin's solution was found to be the best material to clean up the wound. On March 4 there still was little evidence of healing. The gray film (in some places 1 cm. thick) had reappeared. Again this was removed down to bleeding muscle and the entire area was covered with thick split grafts. Again the wound healed over with the gray slough and the grafts were apparently lost. Five weeks later more radical method of closure was

adopted. A large flap of skin and fat, measuring 7 by 4 inches, was removed from the right buttock and swung at right angles to cover the defect. The surface crusted, was again curetted and to our surprise practically all of the skin grafts were present under this hyalinized layer. The grafts were removed and the graft sutured in place. As result of this operation, one-half the wound was closed, for part of the graft sloughed and the rest peeled away. At this time it was noted that three spinous processes were exposed along the edge of the flap which stuck down to the muscle readily.

She was allowed to return home for few months and then reentered the hospital. A large flap was directed up from the left buttock, the irradiation scar and the exposed bone were removed and the flap was sutured in place. This procedure was satisfactory and the wound healed 4 months after the first excision.

During this same period the anterior abdominal wall ulcer was excised and closed by right angle flap 1 sec.



Fig. 6. Case 3. a, left, Irradiation carcinoma following low oblique resection therapy for hyperthyroidism. b, Same after excision and closure by Tidench grafts.

sitting. The necrosis was found to involve all layers of the abdominal wall including the peritoneum, which had the typical gray exudate. Very little difficulty was experienced in the healing of this wound.

### *Group XI Irradiation carcinoma following roentgen therapy for hyperthyroidism*

CASE 23. G. F., age 65, was admitted to the Phillips House on June 8, 1934 with an extensive ulceration over her neck and sternum. Twenty years before she had an enlargement of the thyroid, apparently toxic in nature. She received roentgen therapy in Tennessee, and the tumor decreased in size. The treatments were continued for 18 months and she then developed a "burn" which never healed. For the past 2 years nodules had been appearing in the ulcer.

Examination showed an extensive area of irradiation dermatitis extending from the thyroid cartilage down over the sternum to a point midway between the breasts and about 4 inches wide. The central half was ulcerated and nodular. There were no palpable lymph nodes (Fig. 16).

Operation was done on June 8, 1934. All involved tissues were excised and the wound was left to granulate. At no point did the growth perforate the fascia. Three weeks later Thiersch grafts were applied and healing was uneventful (Fig. 16 b). Microscopical examination showed epidermoid carcinoma, group 2. There was a wide margin of uninvolved tissue at the base of the specimen. Tumor cells invaded the subcutaneous fat. The muscle fibers showed degeneration. This patient has not been followed since operation.

### *Group XII Complications from irradiation of carcinoma of the cervix*

CASE 24. M. I., age 53, was examined at her home June 28, 1938, suffering from cancer of the cervix. A course of roentgen therapy followed by radium was outlined. As she lived near the Pondville cancer hospital she asked that she might have her roentgen therapy as an outpatient. This was agreed to provided she enter the hospital for cystoscopy and intravenous pyelogram before starting therapy. This was done and no abnormality found in the urinary tract. For 10 days she returned for roentgen therapy each day. On the tenth day she complained of pain in the region of her right kidney. An intravenous pyelogram showed marked dilatation of the ureter and kidney pelvis.

This rapid change in the picture was undoubtedly caused by edema of the ureterovesical orifice caused both by the roentgen therapy and the disease process. A ureteral catheter was passed and the treatment was completed with the patient staying in the hospital. Had the condition not been detected early permanent damage to the kidney would have resulted.

CASE 25. I. H., age 59, was admitted to the Pondville Hospital on December 15, 1934. Examination showed a carcinoma which involved the entire cervix and extended onto the anterior vaginal wall. There was no infiltration of the broad ligaments. She was given a course of roentgen treatments to the pelvis followed by two intra uterine radium treatments 5 days apart. She then received a course of roentgen treatments to the perineum.

Six months later she returned, complaining of pain in the rectum and bleeding. An annular, constricting lesion was felt a short distance from the anus with a thick scarred area on the anterior wall. Biopsy showed radiation reaction with scattered cancer cells. No further treatment was given. During the next year she had a decreasing amount of discomfort in the rectum and was comfortable if she took oil. A note was then made that she had a stricture high up which admitted one finger. A year later she showed increasing signs of obstruction. A proctoscope could be passed without difficulty. The rectal mucosa was pale but not ulcerated. She complained of pain around the anus. An alcohol injection into the lumbar subarachnoid space gave slight relief for a time. Two years later an ulceration appeared on the anterior rectal wall below the level of the cervix. Biopsy was negative for carcinoma. The amount of pain increased and a second spinal alcohol injection was done without relief. She lost control of the sphincter entirely after this procedure.

Finally, on October 5, 1940 a colostomy was done. Exploration of the pelvis showed no recurrence of the cancer in the pelvis or in the large bowel. She has obtained relief from her pain.

This patient showed a stricture of the rectum and probably metastatic cancer of the cervix in the rectum 6 months after roentgen and radium treatment. The stricture persisted and an ulceration appeared 5 years after treatment. The satisfactory feature in this case is the apparent cure of the cancer of the cervix and the metastatic area in the rectum.

### SUMMARY

Damage to tissues following irradiation may be due to faulty technique, improper dosage or screening, excessive doses particularly for benign lesions, heavy doses in the successful attack on a malignant growth, or to scattering or penetrating radiation of normal tissues around a malignant growth.

When the circulation of a region is poor, the damaging effect from irradiation is greater. After therapy the circulation becomes poorer in the treated area and any ligation of vessels to that region will result in gangrene of the area. Infection in a treated area may hasten necrosis. The extremities often have deficient circulation and they do not tolerate heavy doses well.

Cancer may develop in an area of irradiation dermatitis after a latent period of as short as 2½ years.

### REFERENCES

1. EWING, Neoplastic Diseases, 4th ed. Philadelphia: W. B. Saunders & Co., 1940.
2. WARREN, S., and SPENCER, J. Radiation reaction in the lung. *Am. J. Roentgenol.*, 1940, 43: 682-701.



In speaking of prophylaxis we refer as a rule chiefly to cervical carcinoma. A possible relationship between a hyperplastic endometrium and a carcinoma of the endometrium has been suggested, but we know of no adequate prophylactic treatment.

In general, education and publicity should be directed toward urging patients to seek earlier treatment and to acquaint the medical profession with the methods of detecting lesions as early as possible.

About one-fourth of all cancers occurring in the female are in connection with the gynecological organs. Because of this high incidence and especially because of the diverse structural composition of the organs involved, no malignant neoplasms in any other location of the body create problems so important of interpretation and at the same time so difficult of solution.

From the therapeutic standpoint, the uninterrupted co-operation of the gynecologist and the radiologist over a long time is necessary to bring about the maximum of achievement. Changes inherent on the improvement of surgical technique are apt to influence radiation procedures, on the other hand, variations in the method of irradiation due chiefly to the continuous development of increasingly more powerful roentgen apparatus cannot remain without effect on surgical considerations.

It is the purpose of this paper to review the cases of patients treated at Harper Hospital from 1922 to 1935 inclusive and to discuss, on the basis of 5 and 10 year survival curves and other statistical figures the more salient points which have left their landmarks on the routine clinical procedures, thus leading to the present day status in the treatment of gynecological cancer. In 1932, a supervoltage roentgen therapy apparatus operating at a voltage as high as 750 kilovolt constant was installed in our institution and since 1933 patients with gynecological cancer have been irradiated with 500-600 kilovolt constant more or less routinely, so that an evaluation of the influence of this change on the 5 year results is also possible for a period of nearly 3 years (1933-1935 inclusive).

The attempt actually to cure carcinoma is of comparatively recent development. While various caustics and cauterizations have been used from time immemorial, the effort to eradicate a malignant disease has been attempted only since the development of surgery. For each type of cancer an operation has been developed. There is no doubt that the lack of any other possible method of cure gave this stimulus to the surgeon to tackle

this problem, and even after the discovery of radium the development of the surgical treatment continued mostly when radium was not available. There is no doubt that the availability or non-availability of radium or x-ray was an influence that affected the plan of treatment. The earlier radical operations for carcinoma of the cervix were developed when radium was unknown or not available. As radium became better known, surgical operations for cervical carcinoma gradually went into the discard. There is now sufficient collected evidence to warrant the statement that the greatest advance in treatment of cervical carcinoma was made when the gynecologist relinquished the surgical treatment for radiation therapy. It is now no longer a question of competition between surgery and radiation, but rather a co-operation. In certain types of carcinoma this co-operation is well shown by the fact that both are employed, especially in carcinoma of the uterine fundus, ovarian carcinoma, and in carcinoma of the external genitals.

#### MATERIAL

The study is based on 845 cases of gynecological cancer of which 636 cases represent carcinoma of the cervix uteri, 77 carcinoma of the fundus uteri, 171 carcinoma of the ovary, and 31 carcinoma of the external genitalia. The cases were all followed up systematically year by year. In tabulating the 5 and 10 year results, attention was paid only to the "survivals." All patients who died from other causes than cancer were assumed to have died from cancer and about 2 per cent of the cases, being untraced, were likewise included among the dead from cancer. Thus the survival curves represent the lowest possible figures and their slight improvement may in time be expected, especially since experience shows that due to the extensive use of the indirect follow-up through the vital statistics bureau, most of the untraced patients are eventually found to be alive. Furthermore, all of the figures included herein represent absolute values. Not one single case was omitted from the compilation of the final results regardless of whether the originally outlined treatment was successfully brought to a conclusion or remained incomplete, and irrespective of whether a patient represented a fair possibility of cure from the beginning or already was in such an advanced stage that palliation could be expected at the best. If only the relative values are considered, making use of well selected groups of cases which are treated according to a program outlined in advance, then, of course, the survival curves assume somewhat higher values.

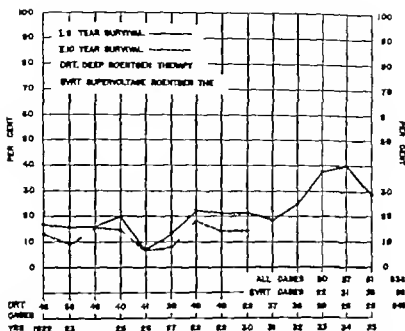


Fig. Survival curves in carcinoma of cervix uteri

## METHOD OF TREATMENT

In the main, an association of surgery and irradiation was used freely and, in preference to either method alone, whenever this was thought desirable.

The surgical technique in this series of cases has varied greatly. In the earlier cases of carcinoma of the cervix we find that panhysterectomy both abdominal and vaginal, as well as the so called Wertheim operation was occasionally performed. In conjunction with these surgical procedures deep roentgen therapy was always administered. Because of the rarity of early diagnosed cases these operations were of unusual incidence rather than the rule. Because of the apparent favorable results retained from radium in some of the advanced cases, the use of this agent gradually replaced surgical operations even in early cases, and it has now been several years since surgical cure of any kind has been attempted.

For carcinoma of the uterine fundus the earlier cases were considered adequately treated when a wide panhysterectomy was performed. Later experience has shown, however, that while this may effect a cure in the lower grades of malignancy it is not adequate for the higher grades of malignancy. Therefore, in the later cases of carcinoma of the uterine fundus, all patients have been treated by both surgery and radiation.

During the course of time all surgical procedures, because of the addition of radiation therapy were reduced to more conservative interventions.

The technique of irradiation consisted in the combination of intracavitary radium and external roentgen therapy whenever possible. From 1921 to 1928, the radium dose varied from 1200 to 2400 milligram hours for a single and from 3600 to 5000 milligram hours for a total application. Since 1928, it has been increased to from 3600 to 5000 milligram hours for a single and from 7200 to 10000 milligram hours for a total application, this change accounting for some improvement in the survival curves, especially as shown in connection with the carcinoma of the cervix. The roentgen therapy was carried out with such an exposure as to obtain the maximum tolerable biological reaction. Apart from minor details, the method of procedure remained essentially the same, but the quality of the rays was changed in 1933. Thus from 1921 to 1932 inclusive, the so called deep roentgen therapy with 300 kilovolts (7 millimeter copper filter) was used and since 1933, supervoltage roentgen therapy with 500 to 600 kilovolts (7 millimeter copper filter) has been substituted for most of the cases of gynecological cancer. The effect of this change is evidenced on the survival curves of each type of gynecological cancer as discussed below.

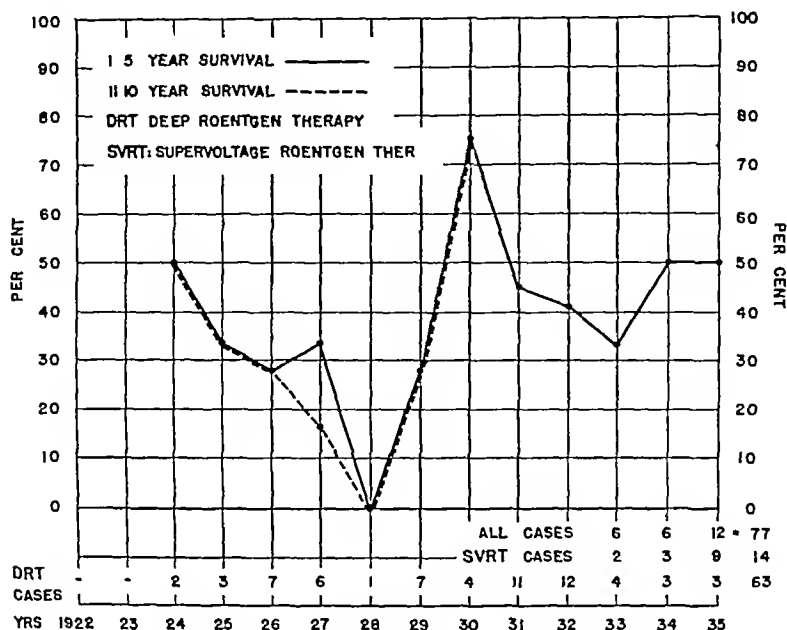


Fig 2 Survival curves in carcinoma of fundus uteri

*1 Carcinoma of cervix uteri* In this group, in the first years as mentioned before, an operation was performed in the early cases and roentgen therapy was used prophylactically, whereas the more advanced cases were treated by a combination of intracavitary radium and external roentgen therapy. During later years, practically all of the cases were subjected to irradiation, and operation was performed only in rare instances. Prior to 1928, the dosage was distributed rather equally between the radium and roentgen rays, but since that year, the intracavitary application of radium has been made the main method, the largest tolerable dose being administered. The roentgen therapy thus became of secondary importance, its aim being merely to make up the deficient dose from the radium around the periphery of the pelvis especially in the regions of the distant parametria. This aim was facilitated since 1933 by the introduction of the more penetrating rays of supervoltage roentgen therapy.

As shown in Figure 1, the 5 and 10 year survivals between 1922 and 1928 averaged 16 and 12 per cent, respectively; from 1928 to 1932, they were raised to 21 and 15 per cent, respectively, and since 1933, the 5 year survivals have reached the average of 35 per cent.

*2 Carcinoma of fundus uteri* In this group, a combination of surgery and radiation therapy was used whenever possible throughout the entire

period. The procedure, as far as the irradiation is concerned, has moved along the same lines as employed in carcinoma of the cervix uteri, and the results are evidenced in the survival curve as shown in Figure 2. As is seen, the average of five year survival has been raised from about 30 per cent prior to 1930 to 45 per cent after that year and to nearly 50 per cent after 1933. The 10 year results here run a rather close parallel to the 5 year results. As already stated, however, these figures represent absolute values and therefore all cases which from the beginning have proved inoperable are included.

In considering separately the operable cases, that is, the group in which a combination of surgery and radiation therapy was used, a sharp line must be drawn between two distinct procedures.

TABLE I — CARCINOMA OF FUNDUS UTERI  
FIVE YEAR SURVIVALS

Method of treatment	Cases treated	Cases well	Percentage
Hysterectomy — postoperative irradiation	36	20	55
Pre operative irradiation + hysterectomy 6 weeks later + postoperative irradiation	7	5	71
Total operable cases	43	25	58
Radiation therapy alone in inoperable cases	34	10	29
Total of all cases	77	35	45



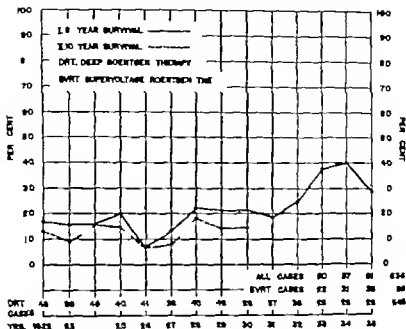


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Thus from 1921 to 1932 inclusive, the so called deep roentgen therapy with 500 kilovolts (1 millimeter copper filter) was used and since 1933 supervoltage roentgen therapy with 500 to 600 kilovolts (7 millimeters copper filter) has been substituted for most of the cases of gynecological cancer. The effect of this change is evidenced on the survival curves of each type of gynecological cancer as discussed below.

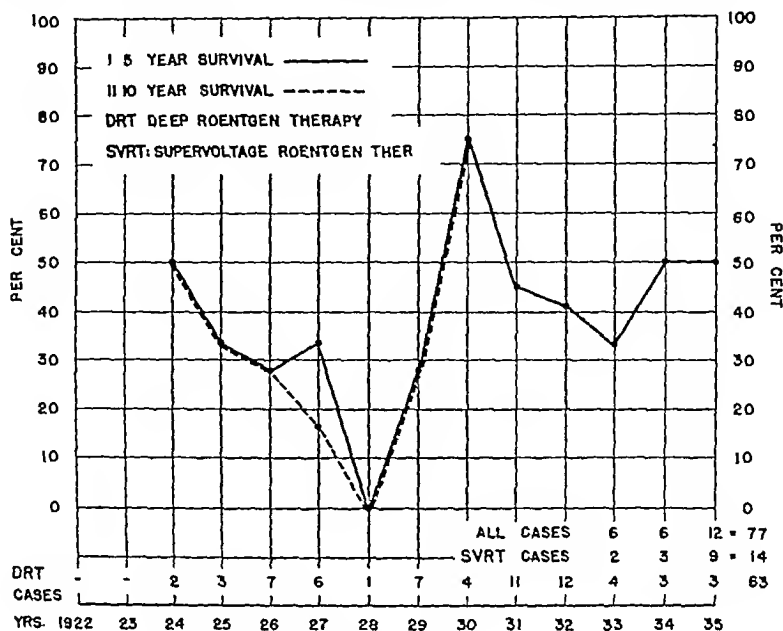


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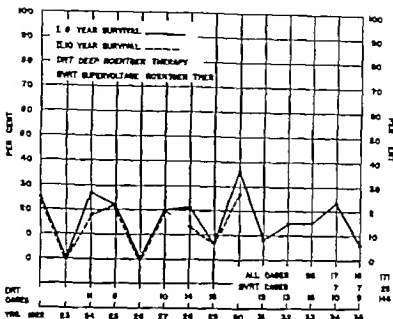


Fig. 3. Survival curves in carcinoma of ovary

In one the operation, consisting mostly of pan hysterectomy was performed as soon as the diagnosis was established and the radiation therapy was administered after operation. In the other a full course of intracavitary radium and external roentgen therapy was given first and the operation performed after the subsidence of the biological effect from the irradiation, usually 6 weeks later. Further irradiation, consisting of roentgen therapy alone was then given in the postoperative period. The results obtained by these procedures are illustrated in Table I. As is seen, whereas a 5 year survival of 55 per cent was obtained in the first, this rose to 71 per cent in the second, the total figure for all operable cases representing 58 per cent.

3. *Carcinoma of ovary* Although the malignant neoplasms pertaining to the ovary may show pathologically diversified appearances, from a clinical standpoint it seems practical to include them under one heading. In most cases, a combination of surgery and radiation therapy was necessary at one time or another. The predominating principle throughout the entire period was that whenever a patient constituted a good operative risk, the large neoplastic masses were removed by surgery and then irradiation was instituted. In other instances, radiation therapy was given in a preliminary way and the operation reserved for the period when the biological reaction

from the irradiation had cleared up. In still other instances, both the operative procedure and the irradiation were repeated or even alternated many times for several years, depending on the clinical course.

As shown in Figure 3, the 5 and 10 year survivals represented broadly 20 and 18 per cent, respectively throughout the entire period. Certainly enough, the addition of supervoltage roentgen therapy in the group treated so far, contrary to expectations, did not seem to have influenced the survival curves. The reason for this is not quite clear and it is possible that with a larger number of cases, the situation might be changed considerably.

4. *Carcinoma of external genitalia.* Of a total of 3 cases of carcinoma of the external genitalia, 14 occurred on the labia, 10 in the vulva, and 7 within the vaginal canal. A combination of surgery and radiation therapy was used in most cases, the technique of procedure being greatly individualized. In carcinoma of the labia and especially of the vaginal canal, at times it was found necessary to rely on the radiation therapy alone. As shown in Table II, the 5 year survivals amounted to 50 per cent for the labia, 10 per cent for the vulva, and none for the vagina. The number of cases treated with supervoltage roentgen therapy is as yet too small to permit an estimation of the value of this method.

## ANALYSIS OF STUDY

In reviewing the results of the above groups several facts become of special interest. The most important, perhaps, among them is that the addition of radiation therapy has greatly changed the conception toward surgical approach. In many instances, operation has become less radical, in others it has been omitted altogether or made an integral part of radiation therapy and again in others the time of intervention has been readjusted so as to utilize the biological effect of the irradiation to the best advantage. In carcinoma of the cervix uteri, for example, surgery is now almost never a factor in curative treatment. In carcinoma of the fundus uteri, surgery continues to play the predominant rôle, but is best performed, after the administration of a full course of radiation therapy as soon as the biological reaction has subsided. There are two reasons why such a procedure is more advantageous. First, the intracavitary application of radium in combination with external roentgen therapy permits a more homogeneous irradiation of the entire pelvis, whereas if the uterus has been removed, the intra-uterine and intracervical insertion of radium, of course, becomes impossible and thus the radiation is, of necessity, less thorough. Second, experimental evidence of Drs. Altemeier and Jones shows that if an operation is performed within 4 to 6 weeks of the irradiation of the peritoneum, there is considerably less danger of infection and thus the postoperative mortality is greatly reduced. It must be mentioned, however, that if the irradiation has been repeated for several series, or given in such a way as to produce considerable fibrosis of the normal structures, then the subsequent operation may become very difficult. In carcinoma of the ovary, surgery may precede radiation therapy or may be undertaken at any time during the course of irradiation. In carcinoma of the external genitalia, the time of intervention and the indications for the two procedures are individualized from case to case. In discussing the surgical aspect perhaps one may also state that because of the not altogether negligible incidence of primary carcinoma in cervical stumps and because of the great limitations in appropriately treating such lesions, the removal of the entire vaginal portion of the cervix may appear advisable whenever a hysterectomy is performed for any other reason. In this way, the removal of the cervix may constitute a prophylactic measure.

Another fact is that irradiation, whenever possible, must be carried out by using a combination of intracavitary radium and external roentgen therapy. When the radium is applied, the prime

TABLE II—CARCINOMA OF EXTERNAL GENITALIA—FIVE YEAR SURVIVALS

Organ	Cases treated	Cases well	Percentage
Labia	14	4	29
Vulva	10	1	10
Vagina	7	—	—
Total	31	5	16

consideration is given to this agent and the dosage is outlined in such a way as to permit its maximum use compatible with the tolerance of the surrounding normal structures. However, since radium alone, unless greatly overdosed, fails to reach the distant portions of the parametrium, it is necessary to make up this deficiency in dosage by the addition of external roentgen exposure. In the cases in which the radium cannot be applied, roentgen therapy becomes the sole method of procedure and hence its dosage must be increased and so adjusted as to meet the diversity of the problems created by the variation in the clinical extent of the malignant process.

A third fact is that supervoltage roentgen therapy seems to acquire an increasing value in the treatment of gynecological cancers. There are at least three reasons, from a physical standpoint, why supervoltage roentgen therapy is considered superior to the deep roentgen therapy. First, there is a greater differential action of the radiation with increasing voltages, permitting the administration of a proportionately larger total dose, second, there is an increase in the total energy which can be delivered to obtain the same skin erythema, and third, there is an increase in the depth dose making a larger absorption at the site of deep seated lesions possible. Clinically this means that a larger total dose can be administered to the carcinoma with lesser injury to the skin and the surrounding structures. The technical procedure becomes simplified and at the same time the homogeneity of the irradiation is increased. The definite curative value of the method, however, will depend very much on the malignancy index of the neoplasm to be irradiated. Only in those instances in which the neoplasm remains of local character for a longer while may one expect any advantage from improving the efficacy of the irradiation, whereas if the malignant process has already produced distant metastases, any form of therapy will remain futile. There is, perhaps, no other field in which these requirements are met as satisfactorily as in the gynecological cancers. Especially is this true of the carcinoma of the cervix uteri in which the neoplastic invasion remains localized in the pelvis for a relatively long time, the fatal complications usually arising from

secondary effects on the neighboring structures or organs (3). If a better distribution of the irradiation can cover the neoplastic area in a more homogeneous manner the chances for an improved result over that obtained with deep roentgen therapy is evident. Indeed a study of the survival curves seems to support such a view. Although the number of patients treated is not yet sufficiently large to warrant final conclusions, nevertheless it appears that the addition of supervoltage roentgen therapy since 1933 has resulted in some rise of the 5 year survival curves in most gynecological cancers.

#### SUMMARY AND CONCLUSIONS

A total of 843 cases of gynecological cancer treated at Harper Hospital during 1922-1935 inclusive was analyzed and the absolute 5 and 10 year survivals studied.

In the main a combination of surgery and radiation therapy was used whenever possible, excepting the carcinoma of the cervix uteri. Of the agents employed for the irradiation, the radium, in the form of intracavitary application with the largest possible doses, was always given prime consideration. The roentgen rays were relegated to the secondary rôle of making up the deficiency of dosage at various points, especially toward the periphery of the irradiated pelvis. The gradual replacement since 1933 of the deep roentgen therapy (300 kilovolt constant, 1 millimeter copper) with the supervoltage roentgen therapy (500 to 600 kilovolt constant, 7 millimeters copper) has not changed this conception. Only the cases not amenable to surgery and unsuitable for intracavitary radium were treated by roentgen therapy alone.

Attention may be called to the following facts for the individual groups:

1. In cancer of the cervix uteri, radiation therapy with few exceptions, constitutes the method of preference. The increase of the radium dose to the maximum tolerable has raised the 5 and 10 year survivals from 6 and 12 per cent to 21 and 35 per cent, respectively and the supplanting of deep roentgen therapy with supervoltage roentgen therapy has now brought up the 5 year survival to practically 35 per cent.

2. In carcinoma of the fundus uteri, and in those cases of carcinoma of the cervix uteri in which a hysterectomy is performed, the optimum time for the operation is within 6 to 10 weeks following the completion of a preliminary series of radiation therapy consisting of intracavitary radium and external roentgen therapy. Further roentgen therapy is given in the postoperative period. By thus proceeding, the 5 year survivals were increased to 71 per cent as compared to 35 per cent when the operation was done first. The absolute 5 year survival of all cases treated since the introduction of supervoltage roentgen therapy approaches 50 per cent.

3. In carcinoma of the ovary a combination or alternation of surgery and radium therapy is used freely. The 5 and 10 year survivals continued to move around 30 and 18 per cent, respectively throughout the entire period. Contrary to expectation, supervoltage roentgen therapy has brought no improvement in the survival curve.

4. In carcinoma of the external genitalia, the indications for operation and radiation therapy are greatly individualized. In lesions around the vulva, operation becomes the major procedure, whereas for skin cancers of the labia and especially the carcinomas of the vaginal canal one may have to rely entirely on radiation therapy. The 5 year survivals for the entire group represent 16 per cent and the 10 year survivals run a close parallel.

All in all, it appears that notable progress has been made in the treatment of gynecological cancer. The absolute survival curves obtained so far though not the apogees of achievement, represent results which can not but encourage us to further increase our efforts in combating this very malignant disease.

The co-operation of the Department of Roentgenology is hereby acknowledged. All radiation data and discussion has been graciously contributed by Dr. Tessa Lewentz, Head of Roentgen therapy.

#### REFERENCES

1. ALTMANER and JOYCE, *J. Am. M. Ass.* 940, 14: 27-30.
2. ACHER and SALL, *Surg. Gynec. & Obst.* 1940, 71: 1.
3. NOTAK, *Gynecological and Obstetrical Pathology*, p. 93. Philadelphia and London: W. B. Saunders Co., 1940.
4. SCHILLER, *Surg. Gynec. & Obst.* 1934, 18: 21.

# FRACTURES AND OTHER TRAUMA

## HOMOLATERAL DILATATION OF THE PUPIL, HOMOLATERAL PARESIS AND BILATERAL MUSCULAR RIGIDITY IN THE DIAGNOSIS OF EXTRADURAL HEMORRHAGE

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**E**XTRADURAL hemorrhage occurs in approximately 3 per cent of the total number of cases of acute head injury. Since the classical paper by Jacobson formulating the modern conception of the clinical syndrome, the diagnosis of extradural hemorrhage has rested in brief upon the sequence of an initial period of unconsciousness following trauma to the head, a lucid interval, the reappearance of loss of consciousness and contralateral paresis commencing in the face or in the upper extremity with or without localized convulsions. In spite of the apparent simplicity of the syndrome, the mortality from this lesion remains unduly high.

In a group of 177 cases collected from the literature during the past 18 years, the mortality attained a level of 56.5 per cent.<sup>1</sup> Even more striking are the statistics of Le Count and Apfelbach and of Vance. These observers studied a total of 1,016 cases of acute head injury at autopsy and in this number observed 165 cases of extradural hemorrhage, the clots from which were considered large enough by these observers to produce appreciable and presumably fatal compression of the brain. Kennedy and Wortis have stated, after a study of similar totals, that "There is a great discrepancy between the number of cases of epidural hemorrhage recognized clinically and the number remaining undiagnosed until they reach the post-mortem table. In our opinion this is due to the fact that the syndrome of epidural hemorrhage is much too rigid."

This high mortality rate may be due in part to concomitant severe injury to cerebral tissue apart

from the extradural hemorrhage. It may be due to the essentially acute character of the hemorrhage and the inability to secure prompt neurosurgical intervention. There remain, however, the indisputable facts emphasized by Kennedy and Wortis that uncomplicated extradural hemorrhage may not conform to the accepted clinical syndrome and that the nonrecognition of such aberrant forms constitutes an important factor in the continual elevation of mortality statistics.

In this paper, 3 selected cases of extradural hemorrhage are discussed as classical or aberrant forms of the same pathological entity and the disturbances responsible for the aberrant forms are pointed out.

**CASE 1** M C, aged 13 years, history no 59,657. Classical form of extradural hemorrhage. History of initial trauma with immediate loss of consciousness for 15 minutes, 28 hours prior to admission. Lucid interval until 10 hours before admission, followed by the slow onset of restlessness, coma, weakness of left upper extremity, dilatation of right pupil, and convulsive movement of left face and left arm. Roentgenogram of the skull was negative for fracture. Right extradural hemorrhage. Operation. Recovery.

While riding a bicycle, patient collided with another cycle rider and fell to the ground, striking the right frontal region of the head with considerable force. A history was secured from the patient at a later date that he was stunned and not completely unconscious, but was cognizant of his surroundings although unable to move. Five minutes after the initial trauma, he was able to walk a number of blocks to his home. He was at once taken to the office of his family physician who sutured a laceration in the right supra-orbital region. He vomited once at this time but was able to walk home where he went to bed. He stated that he recalls nothing of his subsequent course one hour after going to bed. The patient remained restless throughout the night, vomiting frequently, and in the morning could be aroused with difficulty. Approximately 10 hours before admission, restlessness was superseded by an increasingly deeper coma. Convulsive movements were noted at this time about the left side of the face and 5 hours later progressed to involve the left arm and later the left leg.

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<sup>1</sup>See refs 12 17 21 28 31, 32 34 40 41

The admission temperature was 37.6 degrees C., pulse, 60; respirations, 24 and blood pressure 110/85. The patient was deeply comatose, reacting only to extreme pressure over the supra-orbital areas. His reaction to such painful stimuli elicited conspicuous flaccid hemiparesis, involving the left facial musculature, and left arm and leg. There was an ecchymosis over the right temporal region and sutured laceration in the right supra-orbital region. The right pupil was dilated and fixed, the deep tendon reflexes on the left side were subnormal. Routine blood and urine studies were negative. Stereoscopic lateral and anteroposterior views of the skull are negative for any evidence of fracture. A diagnosis of an extradural hemorrhage was made, situated on the right side. The hemorrhage as exposed through small decompression opening, large extradural clot evacuated, and laceration of the main trunk of the middle meningeal artery 3 centimeters distal from the foramen spinosum, as controlled. Four hours following this procedure, the patient, as alert and oriented. On the second postoperative day the neurological examination was negative.

In a chronological consideration of the classical syndrome of extradural hemorrhage the location of the initial trauma is of primary import. Such hemorrhage may occur from rupture of the middle meningeal artery, the accompanying veins, or one of the major venous sinuses, chiefly the longitudinal or sphenoparietal. Obviously, as pointed out by Mellinger and Rawling, bony injury localized to or involving secondarily the squamous portion of the temporal bone is more likely to produce a tear in the middle meningeal artery and associated venous structures. That such a lesion may develop without a bony injury has been pointed out early by Bell and later by Jacobson who presented 8 cases out of 70 without fractures of the skull particularly noted in Cases 2, 3 and 59, and is further confirmed by the case just detailed. In many cases, in which a fracture of the skull is present, ecchymosis and edema in the temporal region arising from linear fracture of the temporal bone correctly suggest the formation of an underlying extradural hemorrhage.

Jacobson particularly emphasized his observation that the lucid interval may show marked variations, and in his cases, the evidence of cerebral compression occurred from 15 minutes to 4 days after the initial trauma. The lucid interval may be completely absent as it was in 32 of 63 cases recorded by Jacobson in which particular attention had been directed toward this detail. Absence of the lucid interval indicates a severe and concomitant cerebral injury or a complicating factor such as alcoholism, and as Verbruggen has noted recently the diagnosis then must rest upon the presence of localizing signs or as has been advised by Dandy and others, upon the use of diagnostic trephine. The length of the lucid interval in uncomplicated extradural hemorrhage in all probability rests upon the rapidity of the

development of the hemorrhage. This in turn is a measure of the type of vascular lesion, be it artery, vein, or sinus, and the resistance to stripping of the dura from the bone (Dandy) or the extent of original shaking of the dura away from the bone (Bell). Characteristically as the lucid interval lapses, bradycardia will develop.

In the majority of cases the expanding clot forms in the temporal fossa adjacent to the vascular tear involving the meningeal artery or veins. In this location and as it expands, the mass causes pressure upon the lateral aspect of the motor cortex causing first a contralateral facial paresis, progressing to involvement of the arm and lastly the leg. Progressive cortical irritation may likewise explain the progressive localized convulsive state. The presence of such a hemiparesis may be elicited in unconscious patients only by extraordinarily painful stimuli. Equally important variations of peripheral motor defect will be discussed in the second and third cases of this report. Confirmatory evidence of the presence of an extradural hemorrhage may be induced from roentgenographic evidence of a fracture line crossing the vascular channel of the middle meningeal artery and from manometric evidence of a high intracranial pressure. Blood in the spinal fluid may or may not be present, depending upon the presence or absence of associated cerebral injury.

CASE 2. M. W. aged 46 years, Lynchburg Hospital, Lynchburg, Virginia. Aberrant force of extradural hemorrhage. History of initial trauma. No lucid interval and persistent loss of consciousness. Laceration of right temporal and left frontal region. Cerebrospinal fluid draining from right ear. Onset of paresis in right face and arm, right, 6 hours after admission. Transient dilatation of right pupil. Left trephine and decompression. Right trephine and removal of extradural hemorrhage. Exits and autopsy. Multiple fractures, base of skull. Subarachnoid hemorrhage. Extradural hemorrhage, operative defect, right. Hemiatonia of hippocampal gyrus, bilateral.

A 46 year old white man was hospitalized, four hours following an automobile accident. History of complete loss of consciousness since the time of the initial trauma. Upon admission, he was semicomatose, responding only to painful and loud auditory stimuli. There are superficial lacerations in the right temporal and left frontal regions of the scalp. There is bloody serous discharge from the right ear. On admission neurological findings were normal and remained so until 6 hours following admission. Then flaccid paresis of the right upper extremity as noted. Fourteen hours after admission, the right-sided paresis involved the face but not the arm, are convulsive movements seen. The patient was examined at this time in consultation by Dr. Harvey Browder of Lynchburg, Virginia, who pointed out during the period of his examination dilated pupil on the right, which reacted sluggishly to light stimulation. This transient dilatation of the right pupil persisted for 30 minutes, and following this time until the patient's death, both pupils remained in mid position, were equal, and reacted normally. The patient's status did not change until 33 hours after admission when the state of



Fig 1 Extradural hematoma, right. Bilateral herniation of hippocampal gyri, more marked on right Case 2

consciousness deepened to complete coma and the body temperature rose to 101 degrees F. A trephine and subtemporal decompression were done on the left side. The brain appeared grossly normal but under extreme tension. The patient's general condition improved until 22 hours later when a second break in compensation occurred, marked by a rise in temperature to 103 degrees, the onset of tachycardia and renewed coma. In this period, there was no change in the neurological status. A trephine on the right side disclosed a large extradural hemorrhage which was removed through a small decompression opening. A rent in the anterior limb of the middle meningeal artery was noted as the probable focus of the hemorrhage. Temporary improvement was manifest following this procedure but exitus occurred 6 to 7 hours after the second operative procedure.

The postmortem examination was restricted to the contents of the cranial cavity. The extradural hemorrhage had been evacuated, but the brain had not filled out the remaining defect, the typical flat depression of the temporal lobe remained. The striking feature of the gross appearance of the brain was the marked herniation of both hippocampal gyri, particularly on the right (Fig 1). Serial sections of the brain showed no obvious change from normal. Due to fixation, microscopic study could not be made. The base of the skull showed a bursting type of fracture with longitudinal involvement of both petrous pyramids, the cribriform plate, and the right occipital bone involving the foramen magnum. The meninges over the base of the brain were filled with bloody fluid.

Earlier recognition of this aberrant form of extradural hemorrhage was rendered difficult by the presence of homolateral hemiplegia and by the failure to interpret the significance of transient dilatation of the homolateral pupil. The significance of unilateral dilatation and fixation of the pupil in individuals with acute head injuries has been a matter of study since the early contributions by MacEwen (26), Hutchinson, and Jacobson. The value of this sign in the presumptive

diagnosis of a traumatic ipsilateral expanding intracranial lesion, extradural or subdural in location, has been abundantly confirmed by the clinical studies of Hoessly, Holman and Scott, and Kaplan, who have directed their studies from this particular point of view. Supportive evidence is present in a mass of papers discussing the subject from a more general point of view. Blakeslee has discussed 610 cases of skull fractures in which 378 manifested pupillary changes. Homolateral dilatation and fixation of the pupil was present in all cases of extradural hemorrhage in this series and frequently occurred in subdural hemorrhage. Wortis and Kennedy noted anisocoria in 220 of 1,000 cases of head injury. In 17 cases of extradural hemorrhage, the authors reported a dilated pupil on the homolateral side in 7, and on the contralateral side in 4. In 42 subdural hematomas, they described a dilated pupil on the homolateral side in 30.

Gurdjian discussed 16 cases of extradural hemorrhage, in 12 of which a dilated pupil was encountered on the homolateral side. McKenzie recorded 20 cases of extradural hemorrhages in which 15 had a homolateral dilated pupil. Jelsma reported 42 cases of subdural hematoma from the literature, in 36 per cent of which the ciliary part of the third nerve was affected. Munro, on the other hand, has stated (32, p 147), "Fixed dilatation of one pupil, usually without demonstrable ptosis of the upper eyelid, occurs often. It is as common opposite the hematoma (subdural) as it is on the same side." On the other hand, in 48 cases of subdural hematoma, noteworthy for the low mortality rate of 4 per cent, Kunkel and Dan-





Fig. Glioma of left temporal lobe. Herniation of hippocampal gyrus. Museum specimen, Duke Pathological Laboratory.

div. recorded anisocoria in but a single case. Pringle stated that a wide, nonreacting pupil is met on the same side as the hemorrhages in some cases. He felt that it was more important that a pupil which is small when the patient is first seen, later becomes wide and nonreacting. Holman and Scott, and Cairns have emphasized the possible transient character of this pupillary reaction.

General agreement appears to exist concerning the significance of a unilateral dilated pupil in acute head injuries, as illustrated again in the first case recorded. That a transient dilatation may be of equally profound localizing import is pointed out by the clinical course of the second case. The mechanism responsible for this phenomenon in acute head injuries has been demonstrated but recently. Macewen (27) Cushing (7) Meyer and Vincent David and Thiebaud have demonstrated ipsilateral herniation of the hippocampus producing pressure upon the third nerve in cases of brain abscess and tumor together with resulting vascular phenomena due to obstruction of the posterior cerebral artery. The regional anatomy and clinical significance of the resulting tentorial pressure cone has been amply discussed and illustrated by Jefferson (18) in cases of brain tumor. Such a herniation in the presence of a temporal lobe tumor is demonstrated in a museum specimen in the Duke Pathological Laboratory: dilated and fixed pupil being recorded in the clinical history (Fig. 2) Hoessly stated from study of his traumatic cases that bilateral dilatation of the pupil was due to central destruction of the sympathetic supply with an accompanying release of the tone of the oculomotor nerve. He felt that uni-

lateral dilatation of the pupil must be due to trauma upon the peripheral portion of the nerve. Blakelee and Cairns stated that unilateral fixed dilatation of the pupil commonly is caused by cortical injury. Kaplan Gurdjila and Holman and Scott have pointed out that the third nerve is peculiarly susceptible to pressure from above and laterally as it progresses toward the superior orbital fissure. McKenzie has discussed four theoretical causes for the phenomena in question. It may be due in the first place to hemorrhage in the brain stem, in the second place from avulsion of the third nerve from the brain stem or pressure of the nerve against the posterior cerebral arteries. He felt that this was the usual explanation for immediate development of the phenomenon. Thirdly, he has explained the disturbance in the majority of cases upon traction of the third nerve around the corner of the clivus by the upper part of the brain stem being pushed to the left, for instance by a right sided hematoma. Finally he mentioned hippocampal herniation but stated that he had not observed it in traumatic cases. Reid and Cone have recently observed such herniation of the hippocampal gyrus in traumatic cases and have confirmed its mechanism by the production of homolateral fixation and dilatation of the pupil by experimental work with monkeys. The *utopian findings* in Case 5 amply confirm this report. Bilateral hippocampal herniation has been described by Olsen with attendant pupillary changes in a case of obscure cerebral edema. The conception of central sympathetic stimulation as the causative agent of homolateral dilatation of the pupil in subdural and extradural hemorrhage has been advanced by Schoercher in a recent publication. It may be stated in summary that in an expanding lesion represented by an extradural hemorrhage, transient or permanent dilatation of the ipsilateral pupil is a significant localizing sign, and that the causal mechanism may rest in herniation of the hippocampal gyrus with pressure upon the third nerve.

In the summary of his paper Jacobson mentioned homolateral paresis as one of seven various manifestations of pyramidal tract defect noted in his cases of extradural hemorrhage, quoting in the body of the paper Case 5 from F. W. Gross. Among modern studies the reports of Rand, Vance and Kennedy and Worth have mentioned this contradictory neurological finding. McKenzie has stated that homolateral paresis in the presence of an extradural hemorrhage indicates contralateral contusion of the cerebral cortex. Munro has

stated, "Furthermore, it is not unknown in the later stages of the slowly developing clot, to have a shifting hemiplegia to the ipsilateral side, with a complete reversal of the expected reflex responses." In the mechanically similar condition of acute or chronic subdural hematoma, Holman and Scott, Fleming and Jones, Frazier, Kunkel and Dandy, and Rand have emphasized this peculiar manifestation of the lesion. Its presence has been attributed variously to pressure upon the crus cerebri, a dilated contralateral ventricle, pressure of the contralateral hemisphere upon the cerebral vault and to contrecoup contusion of the cerebral cortex. In 34 cases of brain tumor with false localizing signs of homolateral paresis or pyramidal irritation, Kernohan and Waltman demonstrated notching of the crus cerebri by the free margin of the tentorium. In the case presented, no satisfactory cause for the homolateral paresis could be demonstrated at autopsy.

**CASE 3** M. C., aged 40 years, history no 32842. Aberrant form of extradural hemorrhage. History of immediate loss of consciousness in automobile accident 30 minutes prior to admission in the course of a prolonged alcoholic debauch. Laceration and contusion of mid-frontal region of scalp. Edema of peri-orbital tissues, left. Persistent loss of consciousness with questionable spasticity and weakness of right sided extremities. Dilatation of left pupil 5 hours after admission. Bilateral spasticity of upper and lower extremities associated with twitching movements. Rapid rise in temperature and pulse with exitus 18 hours after admission. Autopsy: extradural hemorrhage left. Herniation of left hippocampal gyrus.

A 40 year old colored man was admitted 30 minutes following an automobile accident, totally unconscious. A history of "heavy drinking" was obtained, and a strong alcoholic odor was noticed upon examination. A laceration of the left ear, a laceration of the scalp in the midfrontal region and an edematous discolored left eye were described in the admission summary. There was no clinical evidence of a depressed fracture of the skull. Neurological examination was negative. The patient would occasionally mumble and would move all extremities upon painful stimulation. Five hours after admission, stimulation elicited movement of the left sided extremities, but on the right, an early paresis seemed manifest. At this time, the left pupil became dilated and fixed and remained so during the course of his admission. Three hours later, there was marked spasticity in both upper extremities with an unsustained ankle clonus on the right. Active dehydration measures were carried out without relief. There was a rapid rise in temperature and pulse rate and the respiratory rhythm became Cheyne Stokes in character. Fifteen hours following admission, all four extremities were rigid and in extension, although no detailed description of this rigidity is available in the history. Twitching movements of all four extremities are described. Exitus occurred 18 hours following admission.

Autopsy disclosed an extradural hemorrhage, 10 centimeters in diameter and 4 centimeters in width and approximately 3 centimeters in depth in the left temporal fossa with compression of the left hemisphere. There was a linear fracture line in the middle fossa, crossing the vascular channel of the middle meningeal artery 1 centimeter



Fig 3 Extradural hematoma, left. Herniation of hippocampal gyrus. Case 3

from the foramen spinosum, and passing anteriorly across the wing of the sphenoid bone into the supra-orbital plate. Herniation of the left hippocampal gyrus was present with attendant pressure upon the third nerve (Fig 3).

The clinical course of this relatively uncomplicated case of extradural hemorrhage illustrates again several points that have been previously discussed. The lucid interval, which has been unduly emphasized in the classical picture of extradural hemorrhage, may be absent because of associated injury or, as in this case, because of complicating acute alcoholism and the rapid development of the extradural hemorrhage. Homolateral dilatation and fixation of the pupil is represented again as an important localizing sign. Finally, the presence of a relative brachycardia in the second case, and an absolute brachycardia in the first and last cases re-emphasizes the importance (47) of a close observation of pulse, temperature, respiration, and blood pressure reactions as early advised by Jacobson. The classic sequence of events depending upon increasing intracranial pressure as postulated by Kocher and Cushing (6) is well known. The validity of this conception has been challenged recently by Shapiro and Jackson, and by Browder and Meyers, the latter authors stating in their discussion of the classic sequence of events, "In the animal, the physiologic alterations in blood pressure, pulse rate, respiratory rate, and intracranial pressure were produced by pressure applied to the external surface of a brain possessed of an intact vascular tree, whereas in the traumatized human brain the lesion producing the dysfunction is usually intracerebral and is commonly associated with focal or more generalized

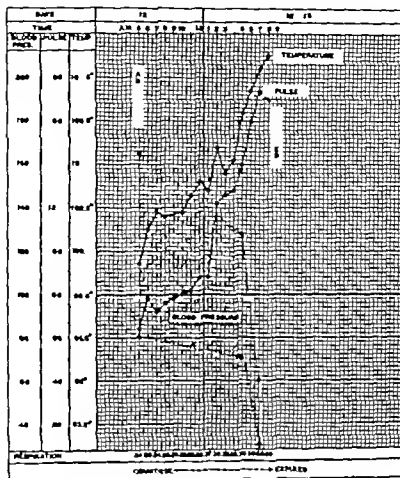


Fig. 4. Extradural hematoma, left. Clinical chart, Case 3.

thromboses of arterioles and venules. Thus it becomes evident that the concept of compression as an explanation of the altered physiologic state of the traumatized patient may be applied in relatively few instances.

The cerebral dysfunction in uncomplicated extradural hemorrhage probably falls into the class of simple compression and proved to be so in the first case recorded as measured by neurological study and lack of postoperative sequelae, and in the third case as measured by histological methods available at the present time for the study of nervous tissue. In all 3 cases reported in this paper the concepts of Kocher and Cushing could be applied with convincing force although it must be acknowledged that repeated measurement of the spinal fluid pressure was not performed (Fig. 4). It is probable that both increased intra-

cranial pressure in these cases represented by an expanding extradural hemorrhage and more subtle pathological intracerebral processes postulated by Browder, may produce the alteration of vital signs detailed by Kocher and Cushing.

The phenomenon of generalized muscular rigidity portrayed in this case has been but infrequently described as a component of the syndrome of extradural hemorrhage, although mentioned by Jacobson in Cases 9 and 39 of his series. It has been observed prior to treatment in one other case of extradural hemorrhage in the Duke Hospital. Jefferson (17) has reported 2 cases in which the usual hemiplegic signs were replaced by a very pronounced degree of generalized muscular rigidity and he refers to the phenomenon as that of decerebrate rigidity citing the paper by Wilson describing the same syndrome appearing in other

circumstances Inasmuch as the description of the rigidity apparent in Case 3 was not further amplified, Jefferson's description of his second case in his report is worthy of quotation

"He was then deeply unconscious, the pupils, of medium size, did not react to light He presented bilateral extensor rigidity of both legs, which were strongly adducted The feet were in full plantar flexion, inversion, and supination Every 3 or 4 minutes the tonic contraction of the limbs became more pronounced, so that the employment of moderate force was insufficient to separate the thighs In the intervals between the attacks the limbs were considerably less rigid, so that the legs could be pulled apart and the knees bent, but at no time was there flaccidity, at no time was there an absence of resistance The left arm during the spasmodic attack was extended stiffly by the side in slight abduction, the wrist was strongly flexed and adducted The fist was nearly, but not quite, closed and the thumb adducted across the palm within the fingers The right arm presented a slightly different picture It was held rigidly bent at the elbow at an angle of 130 degrees, the wrist fully flexed and the hand as on the other side During the tonic seizures both arms rotated inward into a position of hyperpronation so that the backs of the hands were directed toward the thighs On the right side this was largely accomplished by an internal rotation at the shoulder joint, the elbow remaining in partial flexion On the left side, where the whole arm was stiffly held by the side, there was extension and internal rotation of the shoulder aided by pronation in the forearm An attempt to interfere with the limbs during a tonic attack had little effect, and the muscular contraction was so strong that great force was necessary to restrain the movement or correct the position assumed by its agency As in the other case, the tonic attacks were closely bound up with a change in the rate and amplitude of respiration At the height of the attack respiration was rapid, noisy, and deep As far as one could see, the sequence of events was, first, a change in respiration, next, twitching of the fingers on both sides, rigidity, third, there occurred flexion of the wrist and then inversion of the arms the legs and trunk at the same time stiffening into extension During a few of the seizures the patient arched his back in opisthotonos, affecting particularly the lower part of the spine The head was not seen to retract nor to rotate. There was no incontinence. Ankle clonus was rapid and sustained, plantar stimulation led to a bilateral great toe extension, which was very rapid on the right and slower on the left"

Exploration in this patient was carried out in the right frontal region where a depressed fracture of the skull was elevated, autopsy disclosed an extradural hemorrhage on the left. Jefferson stated that the decerebrate rigidity was due to changes in intracranial circulation produced by the injury The same conception of generalized muscular rigidity following trauma to the head has been recorded by Babcock, and he has emphasized the serious prognostic import of the findings Walshe (44) has summarized the characteristics of decerebrate rigidity in man and through such an analysis, has stated that Wilson's cases do not represent true examples of decerebrate rigidity The same criticism may apply to Jefferson's cases when compared to the classical syn-

drome as noted in the case reports of Davis and Walshe (45) The latter author (43) considered the phenomenon as a form of generalized chronic muscular spasm due to direct excitation of gray matter in the pons and medulla from oxygen want, stating that "The irritative symptoms which indicate commencing compression of the brain in traumatic intracranial hemorrhage are associated with cyanosis of the brain, that is, deficient oxygenation and "All the evidence indicates that in the primitive character of sensitivity to oxygen want on the part of the central nervous system, we have a fundamental and potent factor in the production of disordered nervous activity" Whether the phenomenon of generalized muscular rigidity represents decerebrate rigidity or decorticate rigidity or whether it represents simply a premortem rigidity from anoxemia of the medulla, the serious prognostic significance of the finding is clear, and its occurrence in uncomplicated extradural hemorrhage is established

#### CONCLUSION

One classical form and 2 aberrant forms of extradural hemorrhage are described and their neurological and pathological manifestations are discussed in this paper Although Jacobson described aberrant forms of extradural hemorrhage, the modern conception of the clinical syndrome, which had its origin in this paper, is in all probability too rigid The failure to appreciate the various manifestations of the same intracranial lesion may account for the persistent high mortality and for the large number of cases reaching autopsy without clinical recognition A dilated, fixed pupil, either of permanent or transient nature, remains the most valuable lateralizing sign, and may, in many instances, be caused by herniation of the corresponding hippocampal gyrus, with pressure on the third nerve Hemiparesis or other evidence of unilateral pyramidal irritation may be a false localizing sign, caused by pressure of the crus cerebri against the tentorium cerebelli A careful study of the vital signs may aid in the recognition and further study of simple cerebral compression such as that represented by an extradural hemorrhage Generalized muscular rigidity, closely approximating decerebrate rigidity, may occur in simple extradural hemorrhage and represents a serious prognostic sign Its etiology is not established, but may rest upon medullary oxygen want In view of the demonstrable neurological variability of the clinical picture of extradural hemorrhage, it appears advisable to perform bilateral exploratory trephine in all individuals with acute head injuries when the diagnosis is even suggested.

## BIBLIOGRAPHY

- BARCOCK, W. W. Decerebrate rigidity from cerebral injury. *Surg Clin N America*, 1918, 8, 765-768.
- BELL, CHARLES. Surgical Observations, 116, pp. 466-467, cited by Jacobson.
- B. KILPATRICK, G. A. Eye manifestations in fracture of the skull. *Arch Ophthalm*, 1930, 566-57.
- BROWDER, J. and MERRILL, R. A reevaluation of the treatment of head injuries. *Ann Surg*, 1930, 357-375.
- CATENA, H. The ocular manifestations of head injury. *Am J Ophthalm Soc Unit. Kling*, 1929, 49, 3-4, 33.
- CATENA, H. Concerning details regulatory mechanism of the autonomic centre which controls blood pressure during cerebral compression. *Bull Johns Hopkins Hosp*, 1930, 299-302.
- IDEA. Strangulation of the cerebral arteries by lateral branches of the basilar artery in cases of brain tumor. *Brain*, 1930, 53, 704-715.
- D. and W. E. Section on brain. *Practice of Surgery*, edited by Dean Lewis Hagerston, 2nd W. F. Prior Co., 1931.
- D. VIL, L. J. Decerebrate rigidity in man. *Arch Neurol & Psychiat*, 1931, 5, 569-579.
- FLAHERTY, H. W. and JON, O. W. Jr. Chronic subdural hematoma. *Surg Gynec & Obst*, 1931, 54, 8-87.
- FLETCHER, C. H. The surgical management of chronic subdural hematoma. *Ann Surg*, 1935, 67, 680.
- G. KILPATRICK, F. S. Operative management of traumatic intracranial hemorrhage. *Am J Surg*, 1935, 40, 506-6.
- HOMER, H. Das Verhalten der Pupillen beim traumatischen Hirnschaden (Compendio cerebri). *Mitt. d. Grenz. d. Med. Chir*, 1914, 30, 75.
- HOLMES, E. and SCOTT, W. M. J. Significance of unilateral dilatation and fixation of pupil in severe skull injuries. *J Am M Ass*, 1935, 44, 320-332.
- HUTCHINSON, J. London Hosp Rep, 1857, 868, 4. Cited by Verbrughe, loc. cit.
- JACOBSON, W. H. A. On middle meningeal hemorrhage. *Gay's Hosp Rep Series 3*, 339-386, 23, 47-50.
- JACOBSON, G. Bilateral rigidity in middle meningeal hemorrhage. *Brit M J*, 1931, 4, 681-685.
- IDEA. The tentorial pressure cone. *Arch Neurol & Psychiat*, 1935, 40, 857-876.
- JELINEK, F. Chronic subdural hematoma. *Arch Surg*, 1930, 135-141.
- KAPLAN, A. Chronic subdural hematoma: study of eight cases. With special reference to the state of the pupil. *Brain*, 1931, 54, 490-490.
- KRACHT, F. and WOLFE, H. Acute subdural hematoma and acute epidural hemorrhage. *Surg Gynec & Obst*, 1936, 63, 737-74.
- K. VOLLM, J. W. and WALTZ, C. H. W. Injuries of the crura due to contralateral brain tumor. *Arch Neurol & Psychiat*, 1930, 4-257.
- KOCHER, T. Hirnschwellung, Hirnschaden, und chirurgische Eingriffe bei Hirnerkrankungen. *Notnamen! Specielle Pathologie und Therapie*, 1909, 4, 15.
- K. WATTS, F. A. and D. W. E. Subdural hematoma, diagnosis and treatment. *Arch Surg*, 1930, 135, 24-34.
- LE COURT, F. R. and AFFELSON, C. W. Pathologic anatomy of traumatic fractures of cranial bones and concomitant brain injuries. *J Am M Ass*, 1930, 74, 501-5.
- MILNER, W. The pupil in its ophthalmological aspects. *Am J M Sc*, 1887, 94, 3-165.
- IDEA. Pyogenic infections of the Brain and Spinal Cord. Glasgow James Macdonald and Son, 1911.
- M. KROVITZ, K. G. Extradural hemorrhage. *Brit J Surg*, 1935, 26, 346-364.
- M. LANGE, W. J. The base of the skull. With particular reference to fractures. *Ann Otol Rhinol & Laryngol*, 1935, 47, 30, 309.
- MERRILL, A. Hemiatonia of the brain. *Arch Neurol & Psychiat*, 1930, 4, 387-400.
- MOORE, W. B. Traumatic fracture of the cranial bones: clinical considerations, with special reference to extradural hemorrhage. *J Am M Ass*, 1930, 74, 5-5.
- MERRILL, DONALD. Cranio-Cerebral Injuries. London: The Oxford University Press, 1932.
- OLIVER, C. W. Paralysis of the third cranial nerve accompanying increased intracranial pressure. *Bull Los Angeles Neurol Soc*, 1930, 4, 1-17.
- PARSONS, J. H. Traumatic meningeal hemorrhage. With review of seventy-one cases. *Edinburgh M J*, 1935, 45, 74-760.
- R. W. C. W. The significance of dilated pupil on the homolateral hemisphere side in cases of intracranial hemorrhage following head injuries. *Arch Surg*, 1930, 70, 80-80.
- R. W. L. L. B. Head Injuries. London: The Oxford University Press, 1934.
- REED, W. L. and CORN, W. V. The mechanism of fixed dilation of the pupil, resulting from ipsilateral cerebral compression. *J Am M Ass*, 1930, 30, 303-304.
- SCHROEDER, F. Ueber die Ursachen der einseitigen Pupillenerweiterung beim epi- und subduralen Hämorrhagie. *Deutsche Zeitsch. f. Chir*, 1917, 445, 470.
- SILVERMAN, P. and JACOBSON, H. Swelling of the brain in cases of injury to the head. *Arch Surg*, 1930, 135, 433-436.
- V. W. B. M. Fractures of the skull, complications and causes of death: review of 5 necropsies and of 6 cases studied clinically. *Arch Surg*, 1917, 4, 623-69.
- VANDERKAM, A. Extradural hemorrhage. *Am J Surg*, 1917, 37, 275-300.
- VANDERKAM, C. D. VIL, M. and TREIER, U. F. Le rôle de pression temporelle dans les tumeurs des hémisphères cérébraux. Sa symptomatologie et ses traitements qu'il convient de lui opposer. *Rev Neurol*, 1915, 63, 330-345.
- WALLER, F. M. R. The physiology of symptom production in disease and injury of the nervous system. *Brit M J*, 1930, 5, 857-860.
- IDEA. The decerebrate rigidity of Sherrington in man. *Arch Neurol & Psychiat*, 1931, 5, 25.
- IDEA. A case of complete decerebrate rigidity in man. *Lancet*, 1931, 641-647.
- WILSON, S. A. K. On decerebrate rigidity in man and the occurrence of tonic fits. *Brain*, 1930, 43, 20-365.
- WOODHALL, B. M. Acute cerebral injuries: analysis of temperature, pulse, and respiration curves. *Arch Surg*, 1930, 135, 350-375.

# UNDERGRADUATE EDUCATION IN FRACTURES AND OTHER TRAUMAS

CLAY RAY MURRAY, M D, F A C S, New York, New York

FOR a number of years the Committee on Fractures of the American College of Surgeons and now its successor, the Committee on Fractures and Other Traumas, has been attempting to improve the treatment of injury generally throughout this country. As a result of the activities of the numerous regional subcommittees established and kept active in most states of the Union through the untiring and zealous efforts of Dr Charles L. Scudder, by the publication, revisions, and widespread distribution of the *Manual on the Treatment of Fractures* by the general committee with the co-operation of Dr Bowman C. Crowell and the College, and through the nation-wide campaign of the Subcommittee on Emergency Treatment and Transportation under the guidance of Dr Robert H. Kennedy, striking and gratifying improvement in the general handling of the fracture problem has taken place in the last 10 years. There is still much to be done, and the efforts of the general committee and its regional subcommittees will not slacken in the least.

But it has become more and more apparent as the years have passed that a large part of the necessity for the really tremendous effort that this committee has had to put forth lies in the fact that undergraduate instruction in the problems involved in the care of fractures and other traumas has been in general woefully haphazard, unorganized, and frequently distressingly ineffective. Furthermore, instruction in the practical application of the fundamental principles of fracture treatment for internes in our hospitals is frequently lacking or at best on a haphazard basis. More or less voluminous reading and hearsay tested by the "trial and error" method with little or no supervision constitute the fracture education of many of our internes.

Were the treatment of fractures and injury in general a field for the specialist only, the scantiness of instruction for the medical student and the interne would not be of great concern. The

perennial discussion as to whether fracture treatment belongs in the field of general surgery or in the realm of orthopedic surgery is futile and purely philosophic. The great run of fractures have always been treated by the general practitioner—the family doctor. They are now so treated, and, unless I am mistaken, they will continue to be so treated. Nor is there any reason why they should not be so treated. The fractures which require the services of a specialist are those presenting problems which cannot be adequately met except by one who has had special training and experience, and who possesses the necessary technical skill, whether he be a so-called general surgeon or orthopedic surgeon. The general practitioner, the general surgeon who sees few fractures, and the orthopedic surgeon who sees but few should all be able to handle adequately the simple case, and to recognize the case which is unusual and which needs special skill and training at the outset—seeing that it gets into proper hands without delay and without a preliminary period of improper or ineffective treatment.

This broad field of the "average" fracture is, for the most part, in the hands of the "general" man throughout this country. Moreover, and particularly with the younger men just out of school and the hospital, the care of these cases constitutes a respectable portion of their annual income. It is no more a specialized field today than is the treatment of pneumonia, heart disease, or gall-bladder colic. The "specialist" is needed in all these cases, and needed badly, when the unusual case provides the need and the "general" man knows what the indications for this need are. We expect him to know this, we teach him to appreciate it as part of his medical school training. But, we also teach him the basic pathology of the disease, its relation to signs and symptoms, course and prognosis, and the principles of treatment involved. We do this by having him see and examine and follow fresh active clinical cases, by demonstrating the pathology in gross fresh or preserved specimens, and by having him see or help in the treatment of the case. We know we cannot hope to do it by a few didactic lectures and the verbal description of an occasional case to an amphitheater full of students.

From the Department of Surgery, College of Physicians and Surgeons, Columbia University and the Fracture Service of the Presbyterian Hospital.

Presented in the Symposium on Fractures and Other Traumas before the Clinical Congress of the American College of Surgeons, Chicago, October 21-25, 1940.

Obstetrics is another field in which the specialist is, in general, reserved for the unusual case or for those patients whose resources and location make it possible for them to utilize his services from the beginning. These latter constitute the minority. Again, and rightly so we train our students by actual contact with patients—active cases—from the beginning. They see, examine, and help in the treatment of actual patients. Were the curriculum in obstetrics to consist of some didactic lectures, with an occasional amphitheater demonstration of a postpartum case and merely a description of what it had looked like before and during delivery and how delivery had been accomplished, we should rightly feel that medical school instruction in obstetrics was sadly deficient.

The treatment of fractures and other traumas is as much a part of the routine work of the average general practitioner as is the treatment of pneumonia and the handling of obstetrical cases.

Injury has its own peculiar pathology of practical importance from the standpoint of diagnosis and treatment indications. The element of time is peculiarly important. The individual make-up of the patient himself holds a place of importance unusual in other conditions. The whole basis of treatment principles is peculiar to the particular pathology of the condition and is based on that pathology and its time schedule.

A survey of the teaching on the diagnosis and treatment of fractures and other injuries in the medical schools of this country reveals that the didactic lecture the amphitheater demonstration of an all too occasional case—usually after reduction and splinting—with verbal description of what has already been done, and the sometime quizzing on the subject matter of the lectures are the commoner methods of instruction. The number of lectures runs from 3 or 4 to 16 or 17 in different schools. The amphitheater demonstrations from 1 or 2 to half a dozen or more, and the quizzes from none at all to 20 or more. The number of patients seen close at hand before reduction, and the number of reductions and splintings actually so witnessed varies from none in many schools to 20 or more. The opportunity for the student to help in the actual handling of patients varies from zero in some schools to frequent participation in others. In most schools there is no organized course except a lecture series.

In examining men who come up for appointment as internes or who are taking National Board examinations the lack of knowledge displayed on even the fundamental principles involved in the handling of fractures or other

injuries, the vagueness of ideas as to what to do or how or when to do it or why it is done and the total lack of familiarity with what is going on at the site of injury are distressing and deplorable. Certainly a hospital staff should not have to teach its internes the *fundamentals* of pathology symptomatology and the basic principles of treatment.

An aspirant for an Internship who had never examined a chest, or who did not know what a rattle sounded like, or who had nothing to go on except an amphitheater lecture demonstration or examination of the abdomen, or who had no knowledge regarding the significance of the pathology involved in varying types of acute appendicitis would stand little chance of winning a place. Yet, when these applicants are asked how many fresh fractures they have seen, how many they have examined, how many they have seen actually treated and followed, the percentage who answer "none or one" is astounding.

The subcommittee on medical education is attempting to improve this situation. It is not advisable or for that matter necessary at present to ask for more time than is already allowed, at least theoretically in surgery for the teaching of fractures. What is needed now is definite organization of the time allowed so that each student may receive in the course of his four years at a medical school the following instruction: (1) instruction in the correlation between the pathology and repair of fractures and the symptoms and indications for treatment in fractures, (2) instruction in the correlation between the diagnosis and treatment of fractures and gross anatomy, (3) instruction in the basic principles underlying all fracture treatment illustrated by actual patients, as many as possible of whom should be seen by the student while they are receiving their initial treatment, (4) an opportunity to follow some of these patients through the out-patient department long enough to see the results, at least in their early stages, (5) the opportunity if possible, to see some late results on similar patients, (6) actual instruction and practice in the application of the Keller Blake and Murray Jones fixed traction emergency splinting and other forms of emergency splinting, (7) some organized instruction preferably in the sophomore or junior years in first aid in general and in the treatment of trauma in general.

It is also felt that the only way this development can be brought about at the present time is through the individual efforts of the men who are doing the actual teaching.

It is the hope of the Committee on Fractures and Other Traumas that in succeeding years,

through the operation of a number of agencies, we may be able to see the above outline of instruction actually carried out with increasingly frequent close contact with the clinical case. If this can be done, a great advance will have been made, the problems of hospital interne instruction will be simplified, and the need for post-

graduate instruction greatly lessened. The man who is hurt deserves the same consideration as the man who has pneumonia or as the expectant mother. He cannot get it unless his problem is understood. The basic facts of his problem should be an essential feature of undergraduate and hospital interne education.

## RECOGNITION AND EARLY TREATMENT OF INJURIES OF THE GENITO-URINARY SYSTEM

ALEXANDER HAMILTON PEACOCK, M D, F A C S, Seattle, Washington

THE scope of this paper is limited to injuries of the kidney, urinary bladder, and urethra, produced by falls, crushing of the body, and external blows. The deductions and the conclusions were formed from personal experience with 75 cases.

While these injuries comprise but a small percentage of hospital admissions, we are seeing more of them because of the greater number of people carried by motor vehicles and the popularity of vigorous athletics, especially the winter sports.

A serious accident case, especially a patient in shock, presents an immediate diagnostic problem. First, is there a skeletal fracture? A general survey by palpation and roentgenograms should be made, next, a survey of the abdomen is particularly important. Evidences of rigidity, muscle splinting, tumefaction, or localized tenderness give clues to wounded abdominal structure. When hematuria exists the examination should be centered on the kidney, bladder, and urethra.

### THE KIDNEY

The structure of the kidney, particularly, lends itself to injury by a compression blow. Its vascularity is rich, its tissue contains little to hold it together, and its capsule is thin and delicate. Suddenly driven against the lower ribs or the stout vertebrae the kidney may tear easily. The terms, contusion, rupture, and pulverizing, describe varying degrees of injury. Sterling and Sands have demonstrated by animal experimentation just how these injuries take place.

There are some factors in this injury which are favorable to healing. One is the ability of bleed-

ing vessels to close themselves by blood clotting. All surgeons are indebted to this phenomenon. Another is the assistance of shock in temporarily lowering the blood pressure and allowing the terminal vessels to collapse.

The symptoms of kidney rupture are severe localized pain, tenderness, muscle rigidity, and a tumor in the flank. Shock is present in 30 per cent.

Hematuria, to some degree, occurs in all cases. Its source is determined by excretion urography, when the patient is not too shocked. An extravasation of the contrast solution or a failure of excretion in one kidney suggests a rupture. Retrograde pyelograms are more specific and better demonstrate small tears. Many patients with renal injuries are able to endure cystoscopy. Whether to operate early or to watch and wait is a question upon which there is a division of opinion.

Eisendrath and Rolnick reported 26 cases of renal ruptures. Three were operated on and 23 treated without surgery, with 1 death. They strongly advocate conservatism rather than early nephrectomy. The author, in a previous study, reviewed 230 cases, found a mortality of 31.9 per cent for those operated on and 3.2 per cent mortality for those treated without exploration. In my own series of 27 cases, 20 recovered without operation. The mortality of the surgical procedures was 27 per cent.

What is expectant treatment? The patient is closely watched for 72 hours. Hourly blood pressure readings are made, an immediate typing classification for blood transfusion and donors available is made and a blood count is done every 2 hours. Transfusions should be given early, as nothing equals them to hasten clotting and over-



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Fig. 1. Case B. B., male, aged 30 years. Pyelogram showing rupture of middle calyx, right kidney with extravasation of dye, 4 hours after injury.

Fig. 2. Same case. Cystogram showing normal bladder contour, 4 extra minutes 4 hours after injury. Recovery cyst.

coming shock. Severe pain is best relieved by heat and morphine. Intravenous urograms or cystoscopy, catheterization of the ureters, and pyelograms should be done as soon as the patient's condition permits.

One contra-indication to immediate surgery is shock. This is often underestimated. I recall the death of an elderly man who suffered a simple fracture of the femur. Autopsy disclosed nothing else. Surgical curiosity must be guarded against. Experience proves that we can well afford to be patient until the shock of the accident has been counteracted. Should tumefaction, extravasation and infection develop, exploration can then be made. It is amazing to see, at times, a kidney torn in many pieces, yet the hemorrhage stopped by clots.

In cases of vomiting, general abdominal rigidity and severe pain, exploratory laparotomy is justified and indicated.

Two cases will illustrate the importance of early diagnosis and treatment.

**CASE.** B. B., an Oklahoma cowboy, 30 years of age, as brought to King County Hospital on July 9, 1920. At rodeo meet he fell from and was stepped on by his horse. A hoof fractured the sixth to eleventh ribs, right thorax. He suffered considerable pain. The older urine was red, 10th blood. His temperature on admission was 103° degrees F., pulse 90, and blood pressure, systolic 140, diastolic 90 millimeters. The abdomen was soft, except for spasm of the right costovertebral angle. Cystoscopy showed normal locus. The right ureter, jetted blood stained urine, the left clear urine. A right pyelogram using 5 cubic centimeters of contrast solution, showed extra solution of the middle calyx. A cystogram did not show any leakage from the bladder. When

definitely the character of the rupture and that conservative urological treatment, as proper, 13 days hematuria disappeared and on the fourteenth day the patient was discharged. Too early discharge is fraught with danger from delayed hemorrhage.

A case illustrating the more serious type of rupture is the following:

**CASE.** A. J. L., male clerk, 33 years of age, was struck by streetcar 11, as admitted on November 9, 1923, 8 hours after the accident, to Providence Hospital, by Dr. Oscar Proctor. Shock, hematuria, right abdomen, and severe left-sided pain justified an exploration through left rectus incision. Intra-abdominal incisions were found. A large, left retroperitoneal hematoma, as drained through secondary lumbal incision. The kidney as not disturbed. Blood transfusions were administered. The following day the ureters were catheterized. Normal urine flowed from the right one, some from the left. A left pyelogram showed large area of extra solution. As the patient was gaining ground, aiding policy, as followed. Fourteen months later both ureters were catheterized and phenolphthalein intra-urethral gave 5 per cent in 5 minutes from the right kidney, 10 per cent from the left one. One month later the same closed. A renal study, as made recently. Both kidneys function well, though right ectopic and left traumatic hydrocephalus exist.

The secret of success in this patient was certainty at all times of what was transpiring and knowing that the hemorrhage was controlled. The ability of the kidney to recover from the severest of injuries is remarkable and is probably due to its unrivaled blood supply.

#### THE URETER

The ureter is seldom injured by blows. It is small in size, elastic, lies in loose connective tissue and is well protected. It may be torn free

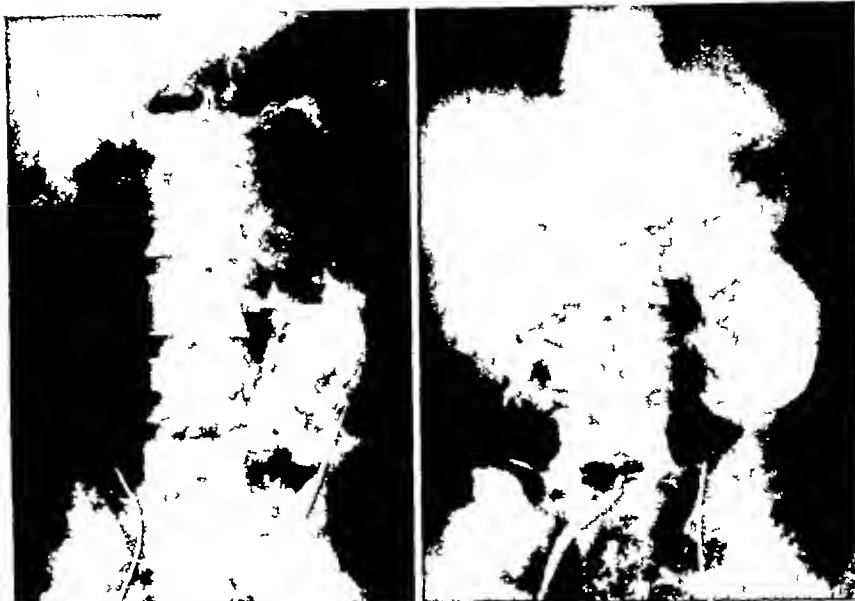


Fig 3, left Case 2 A J L, male, aged 33 years, clerk Run down by automobile Rupture of left kidney with marked extravasation Twenty four hours after injury Recovery 12 months

Fig 4 Same case Rupture of left kidney 2 years later Right ectopic kidney and left traumatic hydronephrosis No symptoms Recovery 12 months

at the renal pelvis It presents few problems in injuries of external origin

#### THE URINARY BLADDER

This organ is frequently injured Two types of injuries are most common When the bladder is distended, a sudden suprapubic blow, as a kick or falling upon the abdomen, may cause an intraperitoneal or extraperitoneal tear The other type, is a puncture of the bladder by sharp bone fragments when the pelvis is fractured These fragments usually cause extravasical extravasation An empty bladder is rarely injured

Out of 28 personal cases of ruptured bladder 20 suffered fracture of the pelvis The cause of accident in this group was 12 due to motor cars, 7 to the logging industry, and 9 to miscellaneous causes

The symptoms vary somewhat, whether intraperitoneal or extraperitoneal extravasation has occurred

When shock or alcoholic intoxication exists early recognition is difficult Suprapubic pain is most significant Suprapubic dullness, hematuria, and low abdominal rigidity require prompt investigation A scout roentgenogram of the pelvis to determine fracture, especially of the ram, and a cystogram will make certain the diagnosis Ac-

cording to Campbell, the mortality of intraperitoneal rupture is high, 73.5 per cent, and that of extraperitoneal, 42.9 per cent, with a corresponding operative mortality Crane reports a mortality of 40 per cent in 26 cases

There should be little delay in determining the patency of the bladder Obtaining clear urine is not conclusive and does not exclude a tear of the bladder wall Weyrauch and Peterfy report recent animal experiments with cystometrograms Their results are not convincing as to this method of determining rupture of the bladder Contrast solution of 5 per cent sodium iodide introduced by a rubber catheter and a cystogram is harmless Air cystograms are less satisfactory Intravenous urography again may not show a rupture If a catheter cannot be introduced an exploratory cystotomy should be made at once The peritoneum should be opened first, looking for intraperitoneal extravasation Next, the bladder should be incised and examined Early cystotomy in all ruptured bladders will cut down the high mortality of this accident Of 28 personal cases 21 had cystotomies with only 2 deaths, 1 after 8 weeks Rupture of the kidney can be treated expectantly but rupture of the bladder, never

CASE 3 R C T, male, 18 years of age, high school student, was referred by Dr Park Willis, Jr, Seattle On



Fig. 5. Case 3. R.C.T. male age 8 years, student. A terrible accident. Cystogram 4 hours after accident showed small leakage from anterior bladder wall. Cystostomy and recovery in 8 weeks.



Fig. 6. Case 4. R.W. male, aged 48 years, houseman. Crushing of pelvis, bilateral fracture of ramus. No cystogram. Rupture of urethra, ischio-perineal extravasation. Death on fourteenth day.

December, 1939, he was thrown from a coupe in collision with second car. He was admitted to King County Hospital 1800 p.m. with blood pressure of 90 systolic and 60 diastolic. Among other symptoms of bodily contusions, he was unable to void. A rubber catheter drew off ounces of bloody urine. He was seen in consultation at 8 p.m. the next morning. The blood pressure was systolic 55, diastolic 70; the shock had passed. An incision obtained 50 cubic centimeters of bloody urine by catheter. There was suprapubic soreness and muscle spasm. Roentgenogram showed separation of pubic bones but no splinters. He was transferred to Seattle General Hospital. At 100 p.m. cystostomy was done, 3 hours after the accident. A tear was found in the anterior wall of the bladder by 3 centimeters, with extravasated extravasation. Drainage by urethral catheter and suprapubic bottom catheter (Fenner). His gaze drains in the prevesical space, completed the operation. After stormy time he was discharged on the forty-second day.

#### THE URETHRA

Injuries of the urethra result from straddle falls, blows, and kicks to the perineum. Others occur when the urethra is torn by a dislocation of the ramus as it passes under the pubic arch. The tube can be sheared off. This disruption may occur at the apex of the prostate. Extravasation

takes place as a rule below Colles' fascia, invading the space of ischio-rectal space, perineum, scrotum, and penis.

These extravasations are particularly vicious and serious infection develops early.

Diagnosis of ruptured urethra rests upon obstruction of the urethra, bleeding from the urinary meatus, inability to micturate, pain in the perineum, marks of trauma, or discoloration and suprapubic dullness and tenderness.

The earlier these cases are seen the better it is for the patient.

Some injuries of the urethra are mild, with no urethral obstruction except edema and very little bleeding. An indwelling catheter will take care of the traumatism. It should be used for a week or 10 days to counteract the formation of scar tissue.

Rupture of the urethra and extravasation require early drainage of the bladder. Some surgeons prefer the perineal, others the suprapubic incision. Most elect the latter. It keeps the scalpel away from edematous, damaged tissue. By the suprapubic route, a sound may be passed through the urethra and to it can be attached a catheter. This is then drawn out through the urethra and acts as a splint, at the point of rupture.

If bladder drainage is not employed early serious complications soon arise—hematoma, infection, abscess formation, and spreading of the extravasation through the triangular ligament. Campbell made a study of 135 cases of peri-urethral infection and noted a mortality of 40 per cent. The longer the extravasation exists, the higher the mortality. Hornaday Beach, and most urologists strongly stress early surgery.

The following case is the usual picture of delayed interference

CASE 4 R W, male, 48 years of age, a longshoreman, was injured by compression of the pelvis. He was caught between two loads of lumber. The injury occurred June 24, 1940. Roentgenograms showed fracture of both rami of the pelvis with displacement. The patient was of large size and the abdomen was distended and tender. A catheter slipped into the urethra and drained clear urine. Later the catheter was withdrawn and he voided. Two weeks after admission, fever, leucocytosis of 23,000 and a swelling of the left inner thigh developed. The following day, July 9, 1940, a perineal incision was made to drain an extravasation. The cavity reached up to the pubic bones, to the site of fracture. The limits of the extravasation were not determined. The patient died the following day and autopsy was not permitted. This patient apparently had a small rupture of the urethra and could have been saved, had an early cystostomy been performed.

It might not be out of place here, to add a word concerning the prevention of these injuries. The motor car has been blamed for many ills yet its use is constantly on the increase. A lesson might be taken from the amusement parks. One of these stunts is a series of small self-propelled cars, guarded by a strong spring-like band, which can bump another car with impunity. The joy rider is further secured by a safety belt. Bumps are the rule but no damage is done. A transportation system, which takes a toll of 40,000 to 50,000 lives a year and injures 200,000, needs some kind of safety study.

#### SUMMARY

- 1 Attention to shock is the first step in treatment of genito-urinary injuries
- 2 Injuries involving the kidney, bladder, and urethra are relatively rare but serious, and always should be considered in general injuries
- 3 Early diagnosis should consist of roentgenograms, urograms, cystograms, and all clinical changes should be carefully recorded
- 4 Tears of renal tissue are frequently self-healing and conservatism is better than too early surgery
- 5 Tears of the urinary bladder and urethra should have early surgery

6 Undiagnosed and undetected extravasation of urine results in a high mortality

7 Motor cars, which are the greatest contributors to serious injuries, need further safeguards, as well as safer drivers

#### BIBLIOGRAPHY

- 1 BEACH, EDWARD W. The so-called straddle injury, its management. *Calif & West Med*, 1937, 46.4
- 2 CAMPBELL, MEREDITH F. *Pediatric Urology* Vol 2, pp 152-190. New York: The Macmillan Co, 1937
- 3 Idem. Perineal phlegmon (urinary extravasation). *Surg, Gynec & Obst*, 1929, 48: 382-389
- 4 Idem. Rupture of the bladder. *Surg, Gynec & Obst.*, 1929, 49: 540-546
- 5 CRANE, JAY J., and SCHENCK, GEORGE F. Rupture of the urinary bladder. *Urol. & Cutan Rev*, 1932, 36: 9
- 6 CREECY, ALBERT A. Injuries of the urinary tract. *Virginia M. Month*, 1940, 67: 542-548
- 7 DOLAN, LEO P. Hematuria and its significance following automobile accidents. *Ohio State M. J.*, 1939, 35: 8
- 8 EISENDRATH, DANIEL N., and ROINICK, HARRY C. *Urology* 4th ed. Philadelphia: J. B. Lippincott Co., 1938
- 9 FARMAN, FRANKLIN. Diagnostic and operative factors in traumatic rupture of the kidney. *J. Am. M. Ass.*, 1940, 114: 210-216
- 10 KINDALL, LLOYD E. Conservative renal surgery with particular reference to kidney trauma. *Calif. & West Med*, 1938, 49: 2
- 11 MATHE, CHARLES P. Traumatic rupture of the bladder. *Calif. & West. Med*, 1935, 42: 5
- 12 PEACOCK, ALEXANDER H. Rupture of the kidney. *West. J. Surg*, 1940
- 13 Idem. Rupture of the urinary bladder. *Northwest Med*, 1940, 39: 7, 248
- 14 PRATHER, GEORGE C. Traumatic condition of the kidney. *J. Am. M. Ass.*, 1940, 114: 207-210
- 15 SARGENT, J. C. Injuries of the kidney. *J. Am. M. Ass.* 1940, 115: 222-226
- 16 SCHENCK, GEORGE F. Traumatic rupture of the kidney. *Calif. & West. Med*, 1934, 40: 5
- 17 STIRLING, W. CALHOUN, and BELT, NORWELL. Traumatic rupture of the bladder with perivesicle extravasation. *J. Am. M. Ass.*, 1929, 92: 2006-2009
- 18 STIRLING, W. CALHOUN, and LANDS, A. M. An experimental study of injuries of the kidney. *J. Urol.*, 1937, 37: 466-479
- 19 WEYRAUCH, JR., H. M., and PETERFY, R. A. Tests for leakage in the early diagnosis of the ruptured bladder. *J. Urol.*, 1940, 44: 3, 264-273



Fig. 5. Case 3. R.C.T. male age 8 years, student. Automobile accident. Cystogram, hours after accident showed small leakage from anterior bladder. All. Cystostomy and recovery in 8 days.

December 930, he as thrown from coupe in collision with second car. He was admitted to King County Hospital at 8:00 p.m. with blood pressure of 90 systolic and 60 diastolic. Among other symptoms of bodily contusions, he was unable to void. A rubber catheter drew off ounces of bloody urine. He was seen in consultation 18:15 in the next morning. The blood pressure was systolic 5, diastolic 70, the shock had passed. An incision obtained 50 cubic centimeters of bloody urine by catheter. There was suprapubic soreness and muscle spasm. Roentgenogram showed separation of pubic bones but no splinters. He was transferred to Seattle General Hospital. At 2:00 p.m., cystostomy was done 3 hours after the accident. A tear was found in the anterior wall of the bladder by 3 centimeters, with extravasical extra action. Drainage by urethral catheter and suprapubic bottom catheter (Pezzer) with gauze drains in the preperitoneal space completed the operation. After stormy time he was discharged on the forty-second day.

#### THE URETHRA

Injuries of the urethra result from straddle falls, blows, and kicks to the perineum. Others occur when the urethra is torn by a dislocation of the ramus as it passes under the pubic arch. The tube can be sheared off. This disruption may occur at the apex of the prostate. Extravasation



Fig. 6. Case 4. R.W. male, aged 48 years, longshoreman. Cracking of pelvis, bilateral fracture of ram. No cystogram. Rupture of urethra, ischioperineal extravasation. Death on fourteenth day.

takes place as a rule below Colles' fascia, invading the tissue of ischiorectal space, perineum, scrotum, and penis.

These extravasations are particularly vicious and serious infection develops early.

Diagnosis of ruptured urethra rests upon obstruction of the urethra, bleeding from the urinary meatus, inability to micturate, pain in the perineum, marks of trauma, or discoloration and suprapubic dullness and tenderness.

The earlier these cases are seen, the better it is for the patient.

Some injuries of the urethra are mild, with no urethral obstruction except edema and very little bleeding. An indwelling catheter will take care of the traumatism. It should be used for a week or 10 days to counteract the formation of scar tissue.

Rupture of the urethra and extravasation require early drainage of the bladder. Some surgeons prefer the perineal, others the suprapubic incision. Most elect the latter. It keeps the scalpel away from edematous, damaged tissue. By the suprapubic route, a sound may be passed through the urethra and to it can be attached a catheter. This is then drawn out through the urethra and acts as a splint, at the point of rupture.

If bladder drainage is not employed early serious complications soon arise—hematoma, infection, abscess formation, and spreading of the extravasation through the triangular ligament. Campbell made a study of 135 cases of perineal infection and noted a mortality of 40 per cent. The longer the extravasation exists, the higher the mortality. Hornaday Beach, and most urologists strongly stress early surgery.

The following case is the usual picture of delayed interference

CASE 4 R W, male, 48 years of age, a longshoreman, was injured by compression of the pelvis. He was caught between two loads of lumber. The injury occurred June 24, 1940. Roentgenograms showed fracture of both rami of the pelvis with displacement. The patient was of large size and the abdomen was distended and tender. A catheter slipped into the urethra and drained clear urine. Later the catheter was withdrawn and he voided. Two weeks after admission, fever, leucocytosis of 23,000 and a swelling of the left inner thigh developed. The following day, July 9, 1940, a perineal incision was made to drain an extravasation. The cavity reached up to the pubic bones, to the site of fracture. The limits of the extravasation were not determined. The patient died the following day and autopsy was not permitted. This patient apparently had a small rupture of the urethra and could have been saved, had an early cystostomy been performed.

It might not be out of place here, to add a word concerning the prevention of these injuries. The motor car has been blamed for many ills yet its use is constantly on the increase. A lesson might be taken from the amusement parks. One of these stunts is a series of small self-propelled cars, guarded by a strong spring-like band, which can bump another car with impunity. The joy rider is further secured by a safety belt. Bumps are the rule but no damage is done. A transportation system, which takes a toll of 40,000 to 50,000 lives a year and injures 200,000, needs some kind of safety study.

#### SUMMARY

- 1 Attention to shock is the first step in treatment of genito-urinary injuries
- 2 Injuries involving the kidney, bladder, and urethra are relatively rare but serious, and always should be considered in general injuries
- 3 Early diagnosis should consist of roentgenograms, urograms, cystograms, and all clinical changes should be carefully recorded
- 4 Tears of renal tissue are frequently self-healing and conservatism is better than too early surgery
- 5 Tears of the urinary bladder and urethra should have early surgery

6 Undiagnosed and undetected extravasation of urine results in a high mortality

7 Motor cars, which are the greatest contributors to serious injuries, need further safeguards, as well as safer drivers

#### BIBLIOGRAPHY

- 1 BEACH, EDWARD W. The so called straddle injury its management. *Calif & West Med* 1937, 46:4
- 2 CAMPBELL, MEREDITH F. *Pediatric Urology*, Vol 2, pp 152-190. New York. The Macmillan Co., 1937
- 3 Idem. Perineurethral phlegmon (urinary extravasation). *Surg, Gynec & Obst*, 1929, 48, 382-389
- 4 Idem. Rupture of the bladder. *Surg, Gynec & Obst*, 1929, 49, 540-546
- 5 CRANE, JAY J., and SCHENCK, GEORGE F. Rupture of the urinary bladder. *Urol & Cutan Rev*, 1937, 36:9
- 6 CREECH, ALBERT A. Injuries of the urinary tract. *Virginia M. Month*, 1940, 67, 547-548
- 7 DOLAN, LEO P. Hematuria and its significance following automobile accidents. *Ohio State M J*, 1939, 35:8
- 8 EISENDRATH, DANIEL N., and ROHNICK, HARRY C. *Urology* 4th ed. Philadelphia. J B Lippincott Co., 1938
- 9 FARMAN, FRANKLIN. Diagnostic and operative factors in traumatic rupture of the kidney. *J Am M Ass*, 1940, 114, 210-216
- 10 KINDALL, LLOYD E. Conservative renal surgery with particular reference to kidney trauma. *Calif & West Med*, 1938, 49:2
- 11 MATHE, CHARLES P. Traumatic rupture of the bladder. *Calif & West. Med*, 1935, 42:5
- 12 PEACOCK, ALEXANDER H. Rupture of the kidney. *West J Surg*, 1940
- 13 Idem. Rupture of the urinary bladder. *Northwest Med*, 1940, 39, 7, 248
- 14 PRATHER, GEORGE C. Traumatic condition of the kidney. *J Am M Ass*, 1940, 114, 207-210
- 15 SARGENT, J C. Injuries of the kidney. *J Am M Ass* 1940, 115, 222-226
- 16 SCHENCK, GEORGE F. Traumatic rupture of the kidney. *Calif & West. Med*, 1934, 40:5
- 17 STIRLING, W. CALHOUN, and BELT, NORWELL. Traumatic rupture of the bladder with pericystic extravasation. *J Am M Ass*, 1929, 92, 2006-2009
- 18 STIRLING, W. CALHOUN, and LANDS, A M. An experimental study of injuries of the kidney. *J Urol*, 1937, 37, 466-479
- 19 WEYRAUCH, JR., H M., and PETEPHY, P A. Tests for leakage in the early diagnosis of the rupture of bladder. *J Urol*, 1940, 44, 3, 264-273



## FRACTURES DUE TO MUSCULAR VIOLENCE

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**I**N discussing the subject of fractures recently with some of my colleagues, I found that although they had had a rather large experience with fractures they had not actually seen many instances in which the fracture was produced by true muscular action or violence. A review of a number of recent books and of the literature dealing with the subject revealed that while the opinion exists that various types of fractures may be caused by muscular action or violence only a very few descriptions or roentgenograms of such fractures appear in these articles or books. With fractures due to muscular violence I do not include those fairly common, small chip fractures seen at muscular origins or attachments. I refer to the more extensive fractures produced entirely by muscular action in the absence of direct or indirect violence.

I will discuss first 4 cases of fracture of the humerus in the lower third, spiral or comminuted in type, 3 of which were caused by throwing a baseball, 2 by throwing a soft baseball and 1 by throwing a regulation baseball.

In the first case a man 3 years of age while playing in a soft ball game threw the ball from first base to third base and in doing so fractured the right humerus in the lower third. He heard the bone break and immediately had radial nerve symptoms—numbness and partial paralysis—which later cleared up.

The second case was a fracture of the left humerus in a young woman, who in falling forcibly extended the arm in an effort to catch herself but came in contact with no object.

I consider that in both of these cases the action of the muscles in the shoulder girdle in combination with those of the upper arm, was the causative factor in producing the injury. The whipping or snapping action of the forearm in the process of throwing while the arm was in abduction was factor in producing the fracture. In the woman, to a certain extent, the muscular action may not have been as great as that necessary to throw the ball in the first case yet the arm was abducted and forcibly extended, so I believe that the forcible extension of the arm was one of the chief factors in producing the fracture.

These two fractures were of the comminuted type and both had marked radial nerve involvement. In both cases I used the Thomas arm splint, inserted a Kirschner wire through the olecranon under cyclopropane anesthesia, and applied 8 to 10 pounds of traction. The patients were kept in bed. My reason for using this type of treatment was to prevent further radial nerve damage by the continued traction and to prevent if possible the extensive throwing out of callus. After 4 to 5 weeks the arms were put up in plaster-of-Paris casts from shoulder to finger tip, with the elbow at right angles. As union in both of these cases was slightly delayed, the weight of the cast also helped to maintain the position. Both patients obtained good results.

The third patient another fracture due to throwing baseball was treated by Dr. E. S. Allen. While pitching the ball the patient suffered a spiral fracture of the right humerus, lower third. It was reduced under novocain infiltration anesthesia. There was no comminution but there were radial nerve symptoms. The arm was placed in a Zimmer splint with the elbow at right angles. The bone united well and there was no permanent nerve involvement. Unfortunately the original ray films in this case were destroyed, but we do have a copy of the x-ray report made by Drs. Keith and Keith, which follows:

Right humerus. Films of the lower half of the right humerus, including the elbow joint, show a spiral oblique fracture 3 inches in length, the center of the fracture being approximately 5 inches above the elbow joint. The distal fragment is rotated and displaced posteriorly approximately 1 centimeter and there is approximately 1 centimeter overlapping.

Fluoroscopic observation after infiltration novocain anesthesia and several attempts at reduction and several fluoroscopic observations, the arm being fixed in Zimmer splint, show good alignment and good approximation of the fragments. No overlapping.

After permanent dressing had been applied the arm as observed. The patient is supine and erect positions, and it appears good reduction has been maintained.

Dr. Charles F. Wood, one of our orthopedic surgeons has permitted me to report, as our fourth case his personal experience with this type of fracture. While attending medical school, Dr. Wood played soft ball. While pitching one time he felt and heard his right humerus fracture in the lower third. The fracture was spiral in type



Fig 1 Case 1 a, Anteroposterior and lateral views at time of injury, fracture at the lower third of the humerus, due to throwing a ball b, The result of traction after the application of a Kirschner wire through the olecranon c, Anteroposterior and lateral views taken 4 weeks, and,

d, 6 weeks, after application of traction e and f, anteroposterior and lateral views 1 year after injury, g and h, photographs to show function of the arm and hand 1 year after injury Radial nerve symptoms which accompanied the fracture later cleared up

and was associated with a marked and persistent radial nerve involvement, which in the course of time cleared up Dr Yandell Roberts had placed the arm at right angles in a plaster-of-Paris dressing, with excellent results Unfortunately, we can present roentgenograms showing the fracture only as it is at the present time

The four fractures presented are of a rare type, and I have seen no complete description of them in the literature While all were complicated by radial nerve involvement, either tingling in the fingers or a partial paralysis, fortunately, the nerve involvement required no surgical intervention and cleared up in all cases

A fifth case of fracture due to muscular action was seen in a structural steel worker The man was in a sitting position with his back braced and was helping to push a steel beam into position, with his left leg flexed at the knee, while pushing he felt his patella crack and give way with acute pain in the knee joint The man had a transverse fracture of the patella, the result of forcible contraction of the quadriceps femoris muscle It was treated by the usual open surgical operation, and the leg was put up in a plaster-of-Paris cast He made an uneventful recovery with a good result

The sixth and last case was that of a young farmer who had a small rural trucking business



b



d

Fig. 2.



Fig. 3.

Fig. 4.

(Legend on opposite page)

Fig. 5.

One of his trucks became stuck in a mud hole. While pushing against the truck, he felt something give way in the left lumbar region of his back. This was followed by acute pain. At first he thought he had lumbago, but eventually a roentgenogram of his spine revealed fractures of the transverse processes on the left side produced by forcible contraction of the psoas quadratus lumborum and the longissimus dorsi muscles. The patient was treated by rest on a Bradford frame, followed by the application of a back brace. He made an uneventful recovery.

Along with the mechanical treatment patients are given a high calcium diet, super D cod liver oil, diacalcium phosphate vials. Blood calcium estimations, complete blood counts, Wassermann and Kahn tests are made. When it is deemed necessary, basal metabolism readings are also made to determine the dosage of thyroid necessary. We also use all indicated types of physical

therapy: massage, diathermy, whirlpool baths, etc.

I have seen no compound fractures due to muscular action. If they were encountered, however, I believe we should treat them as other compound fractures, with gas and tetanus antitoxin, x-ray therapy, sulfanilamide, sulfathiazol, along with properly recognized surgical procedures. I believe that x-ray therapy has a definite place in the treatment of compound fractures whether gas or pyogenic infection is suspected. It apparently does not delay bone union when given in proper dosage. I have had no experience with Dr. Trautman's method of treatment as developed in the late Spanish war.

#### CONCLUSIONS

Fractures due to muscular violence are not as common as one would suspect. In our series of cases the fractures all occurred in young patients during the period of life when muscular violence is most common.

Fractures of the humerus which are produced by the throwing of a ball are fairly rare; many surgeons of large experience have never seen a case.

All fractures should be seriously regarded, and just as in other medical and surgical conditions all diagnostic methods should be used to determine the extent of the injury and thus to arrive at a decision as to the proper treatment to use in a given case.

I wish to express my thanks to Dr. J. S. Allen and Dr. Charles L. Wood for permitting me to add their cases to this report.

Fig. 1. a. Roentgenogram taken at time of injury. Case 1. b. Roentgenogram taken after traction had been applied by Kirschner wire through olecranon with arm in Thomas arm splint. c. Patient in bed showing method of traction of fracture comm. into position under traction. e. Anteroposterior and lateral views 4 months after injury. Beginning callus formation, delayed union. f. Type of plaster dressing worn following the old principle of permitting weight of cast to help maintain position of fracture.

Fig. 2. Case 4. Result (Dr. Wood) at present time. Fracture over third of humerus due to throwing soft ball.

Fig. 3. Case 5. Transverse fracture of patella in young steel worker due to forcible contraction of the quadriceps femoris muscle.

Fig. 4. Case 6. Fracture of transverse processes due to contraction of psoas quadratus lumborum and the longissimus dorsi muscles.

# FRACTURES INVOLVING THE ANKLE JOINT

## A Classification Based Upon Pathology and Indications for Treatment

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THE subject of ankle fractures, which, for the purpose of this discussion will include only those injuries of the ankle joint in which the lower end of either the tibia or fibula is fractured with or without displacement of the astragalus, has been well described and is understood by those who have taken any particular interest in the matter.

Ashhurst has classified these fractures into four groups: (1) fractures due to external rotation of the foot; (2) fractures due to abduction of the foot; (3) fractures due to adduction of the foot; (4) compression type of fractures. This is a most excellent classification, and one with which we cannot disagree in any way at all. As a matter of fact, it is such a good classification that it has been copied in most recent textbooks on fractures. However, after watching a good many groups of internes through their hospital year and discussing the matter with a large number of recent graduates and general practitioners, I believe that the average doctor has a very hazy idea of these injuries. He usually remembers something about a Pott's fracture and is inclined to apply this term and the treatment for the Pott's fracture to practically every injury which occurs within the ankle. This situation combined with the additional fact that many of these patients are semi-ambulatory from the beginning and frequently are taken to the office of the nearest doctor rather than to a well equipped hospital, has led to too many disastrous results.

We believe that the reason internes have so much difficulty in remembering the Ashhurst classification is because it is predicated upon the types of force applied to the ankle rather than upon what has happened to the ankle and to the additional fact that several types of injury are included in each of Ashhurst's groups. External rotation we know may cause a Pott's type of fracture and also may cause a Cotton's type. While the same force may have caused one or the other of two injuries, the type of treatment required is totally different. And, of course, there is also the additional fact that the history is often

difficult to get and sometimes not truthful. The result is that the interne, being unable to get a reasonably good story, jumps to the roentgenogram as his only means of diagnosis, forgetting that palpation of the bony landmarks will give almost as much information as any other form of examination. Again, many of these patients are taken to the office of a doctor who has not the benefit of an x-ray machine and if it appears to be an injury in which the displacement is slight, the condition may be called a sprain of the ankle.

It seems to us, then, that a classification based on the structures injured and the displacement which will or has resulted from the accident is one which would be more easily remembered. If one considers that all fractures of the ankle are produced by forces so applied that the astragalus is forced or rotated from its normal position with fractures of one or more bony parts of the mortise or rupture of the soft tissues which hold it in position, we can establish at once five types of fractures. They are:

Fractures with outward displacement or rotation of the astragalus, or fibular flexion or abduction whichever term one wishes. This, of course, would include the Dupuytren's and the Pott's, either with fracture of the internal malleolus or rupture of the deltoid ligament.

2. Fractures with inward displacement or rotation of the astragalus, or tibial flexion or adduction fractures. These fractures usually are of the bimalleolar type.

3. Fractures with backward displacement of the astragalus, or the Cotton's type of fracture, whether initiated by a straight backward force or rotation, but in which backward displacement of the astragalus is the prime feature.

4. Fractures with forward displacement of the astragalus, a rare type, but one of which we ourselves have four examples.

5. Fractures with upward displacement of the astragalus.

In our experience all fractures caused by rotation fall into one or the other of these groups. Of course, there are many instances in which the displacement is slight or nil, but it should not be difficult to classify such a case and to select a method of treatment which is suitable. We all

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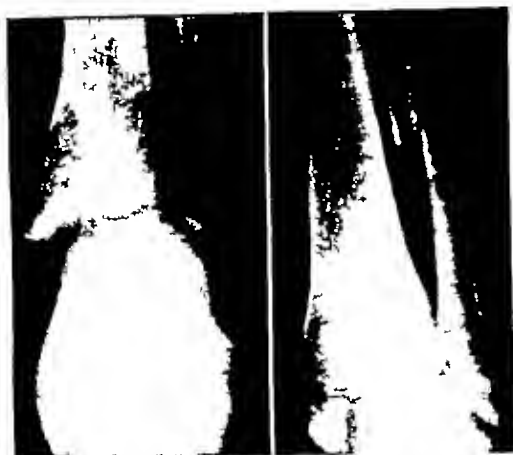


Fig 1 Two examples of fracture with external displacement of the astragalus a, left The internal lateral ligament has been ruptured b, The internal malleolus has been fractured Reposition of the astragalus to its normal position is necessary in either case



Fig 2 Fracture with internal rotation of the astragalus (bimalleolar fracture with marked supination of the foot)

know, of course, that in the Pott's fracture the internal lateral ligament may be torn rather than the internal malleolus fractured And, in case of backward displacement, again the posterior malleolus of the tibia may not be fractured, but, in any case, replacement of the astragalus to its normal position will cause the fragments of bone and soft tissue to fall into place

Key and Conwell follow this classification in the opening paragraph of their discussion of ankle fractures, but then list the classification of Ashhurst as given above We have no quarrel with this Ashhurst classification, but, as stated, it seems to us that it is confusing to students and internes

Diagnosis is accomplished by four methods (1) observation of the deformity, (2) palpation of the bony landmarks and elicitation of points of tenderness, (3) history, which may be difficult to get truthfully and may come only after leading questions, (4) the roentgenogram, which should never be neglected, but the diagnosis should be made before the plates are viewed

#### *Treatment*

The primary principles of treatment of any of these cases include, first, an accurate reduction, and second, some means of splinting the ankle and maintaining this reduction until union has occurred Getting an accurate reduction, of course, means pulling the foot and astragalus back into position in the reverse direction from which it went out of place That is, in type 1, shoving

the foot and astragalus to the inner side, in type 2, shoving it to the outer side, in type 3, bringing it forward, in type 4, backward, and in type 5, downward If there is any rotation in connection with any one of these deformities, that, then, must be corrected at the same time Generally speaking, however, all of these patients fall into two groups in regard to treatment

Types 1, 2 and 4, that is, the types with displacement toward the inner side, displacement toward the outer side, and displacement forward lend themselves very nicely to manipulations under local anesthetic The patient can be sat up

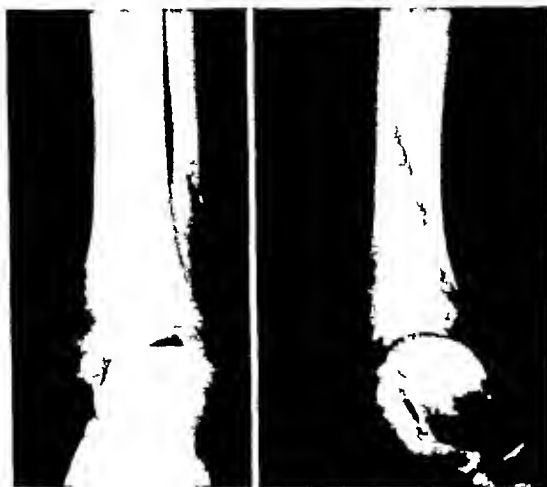


Fig 3 Fracture with forward displacement of the astragalus



Fig. 4. Fracture with backward displacement of the astragalus (Cotton's fracture). a, The fracture unreduced. b, The fracture only partially reduced. It can be seen that the astragalus will slip off the edge of the tibia with very slight movement. c, The astragalus brought still further forward gives better reduction.

while this is being carried out, and a skin cast can be applied with the foot in normal relation to the leg and the ankle at 90 degrees. Of course, in compound fractures or in simple fractures in which the skin is in bad condition, skin casts

should not be used. If it is necessary to use a padded cast, overcorrection must be carried out. If a skin cast is used successfully a walking iron can be applied and the patient made ambulatory early, but if a padded cast is necessary a walking



Fig. 5. Fracture with astragalus driven up and between the tibia and fibula. a, left, Before reduction. b, After reduction.



Fig. 6. T shaped fracture of the tibia with the astragalus driven up and between the fragments. Skeletal traction as necessary to get this reduced.

iron is not advisable. X-ray films should be made as soon as the plaster is set, and if the reduction is not satisfactory it should be done over.

In cases of type 3, that is, the backward displacement group or Cotton's fracture, however, it is very difficult to get reduction by manipulation alone, and it is very difficult to maintain the reduction while a cast is being applied. This is particularly true with a local anesthetic, for it must be remembered that if the posterior lip of the tibia is broken off the astragalus slips about upon what is left of the lower end of the tibia very easily. It is very difficult to get a reduction in the first place unless a patient is thoroughly relaxed. We have therefore learned to go immediately to the general anesthetic. The patient can be handled best when he is lying on his face, the knee bent at a right angle, and then with someone holding the leg, the fracture reduced by pulling the foot forward and holding it in that position with the greatest degree of dorsiflexion of the ankle possible, while a plaster cast is being applied. Even with a good anesthetic and a good assistant, it is not always possible to hold the fragments in position long enough to get a cast set. If, after one good honest try, our immediate films show us that we have failed, we think it best immediately to put a pin through the os calcis. Then, with the knee bent at 90 degrees over a frame, to put on strong skeletal traction and at the same time press backward on the leg and forward on the heel, thus get reduction. A cast is applied at once, but the traction is maintained after the patient is returned to bed, the leg having been placed on a bent Thomas or Braun's frame. After about 3 weeks, there is usually enough callus present so that traction can be eliminated and later the pin removed. Even then we do not permit a patient to walk with a walking iron, for we have seen redisplacement of the fragments occur in these cases even in a well fitting cast. We have heard it said that the only way to get these fractures reduced is to cut the tendo achillis. But with this statement we cannot agree. The tendo achillis is long enough in the first place and will be long enough again. However one must get a high degree of anesthesia for if there is spasticity of the gastrocnemius reduction is impossible. It is further necessary always to put these ankles up with the foot dorsiflexed to the greatest possible degree.

The type 5, or compression type of fractures, are caused by falling from a height, the patient landing on his foot, in which case neither the os calcis nor the astragalus is fractured, but the whole force taken up by the lower end of the tibia. Sometimes the tibia and fibula are separated and the astragalus is driven up between these bones. Sometimes there is a T shaped fracture of the lower end of the tibia with the astragalus driven up between the fragments of the tibia, these fragments lying in front and behind the astragalus, and sometimes only a typical Cotton's fracture is produced. Skeletal traction, as described above, is generally necessary to get reduction in cases of compression fractures. A skin or padded cast is used, depending on the condition of the skin. If a padded cast is necessary, the pin must be left in for a longer time than if a skin cast were used. The walking iron should not be applied until union is fairly firm.

There are cases, of course, which may have been caused by any one of several forces in which there is no displacement. These, if the skin will stand it, are best treated with a plaster cast with the foot in normal position.

#### CONCLUSIONS

We, therefore, wish to present a classification of these injuries, according to the damage which has occurred, regardless of what force has caused it. We realize it is not as scientific as the Ashhurst classification, but we believe it is one which the average student and interne is more likely to remember. Further than this, the methods of reduction and the indications for treatment are suggested in this classification.

#### BIBLIOGRAPHY

1. CAMPBELL, WILLIS C. A Textbook on Orthopedic Surgery. Philadelphia and London W. B. Saunders 1930.
2. COTTON, FELDER J. Dislocations and Joint Fractures. 4th ed. Philadelphia and London W. B. Saunders 1924.
3. KEE, J. ALBERT and CONWELL, H. LAFLE. The Management of Fractures, Dislocations, and Sprains. St. Louis The C. V. Mosby Co. 1934.
4. SCODDIE, CHARLES I. The Treatment of Fractures. 10th ed. Philadelphia and London W. B. Saunders Co. 1926.
5. WILSON, PHILIP D. and COCHRAN, WILLIAM A. Fractures and Dislocations. Philadelphia J. B. Lippincott Co. 1915.



Trueta, relating his experiences with the Orr method in the treatment of compound fractures at the Base Hospital in Barcelona, have been so astoundingly satisfactory that this technique demands renewed interest and consideration. The Orr method is certainly far more readily carried out than the method requiring skeletal traction with the extremity immobilized on a Braun-Boehler splint. The Orr method requires less subsequent dressings, so that in military practice, especially it would seem to be more practical.

During the first phase of the present war in 1918 at the U. S. Hospital No. 38 at Nantes, compound fractures were treated by wound débridement and the installation of Dakin's solution after the Carrel technique with the employment of the Hodgson or Thomas splint. We employed soft tissue traction. No skeletal traction was used at that time. It may be readily appreciated that if the devitalized soft tissues of such compound fractures can be débrided and the extremity immediately immobilized with plaster of Paris, the treatment in military surgery would be greatly facilitated.

Trueta's book is certainly a valuable addition to our knowledge of the treatment of fractures. Whereas it does not advocate any new treatment, yet it certainly emphasizes the value of the conservative Orr method.

#### BI-MALLEOLAR FRACTURES

Other types of fractures of the lower leg which have been satisfactorily treated with the skeletal traction and the employment of the Braun-Boehler splint, are the bi-malleolar fractures and the Pott's fractures, especially when complicated with upward displacement of the astragalus. In these types of fracture we again advocate skeletal traction with a Kirschner wire through the os calcis and the employment of a Braun-Boehler splint.

All cases of fracture of both bones of the lower leg are treated during convalescence with the use of a weight-bearing brace. Our time of bony union has been greatly hastened by the employment of the weight-bearing brace. We have had no case of nonunion—that is, in those cases which we treated from the incipency of the injury. We believe however that such a weight-bearing

brace should extend to the thigh, not merely to below the knee.

The average length of time from the infliction of the injury to the application of the weight-bearing brace is about 8 or 9 weeks for fractures of the shafts of the tibia and fibula, and 10 to 12 weeks for bi-malleolar fractures. To allow weight-bearing prior to 10 or 12 weeks for bi-malleolar fractures, especially if patient is heavy or obese, increases the danger of a resulting wide, painful, weak ankle.

#### CONCLUSIONS

Skeletal traction with the employment of a Kirschner wire through the os calcis, the leg being placed in a Braun-Boehler splint, has been satisfactorily employed in fractures of the tibia and fibula such fractures include "bumper" or "fender" fractures, transverse, oblique, and spiral fractures of the shaft of the tibia associated with fractures of the fibula as well as bi-malleolar fractures and Pott's fractures complicated with upper dislocation of the astragalus. The treatment has been used for both simple and compound fractures. It is not as radical as the open reduction method with internal fixation. The method is not difficult to apply and does not require the experienced technique of open reduction. In compound fractures the method allows easy access for the treatment of the wound.

In all fractures of both bones of the lower leg the use of a weight-bearing brace during convalescence is strongly advocated.

#### BIBLIOGRAPHY

- BOEHLER: Treatment of Fractures. Baltimore: William Wood & Co. 1935.
- BRIDGEMAN: Northwest Med. 1938, 37, 62.
- CALDWELL: Arch. Surg. 1937, 35, 968.
- COTTON AND BIRN: New England J. Med. 1940, 382, 660.
- CURRIE: Surg., Gynec. & Obst. 1934, 59, 46.
- DYER: Am. J. Surg. 1937, 53, 70.
- DYER: Surg., Gynec. & Obst. 1937, 65, 690.
- ELIASON: Surg., Gynec. & Obst. 1933, 57, 653-667.
- FORRESTER: Am. J. Surg. 1933, 30.
- ORR, H. WINSITT: Arch. Surg. 1940, 40, 837.
- TERRY: Treatment of War Wounds and Fractures with Reference to Closed Method as Used in the War in Spain. New York: Paul B. Hoeber, Inc. 1940.
- WICK: A Textbook of Surgery. Edited by Frederick Christopher. P. 693, 3d rev. ed. Philadelphia and London: W. B. Saunders Co., 1939.
- WINTERLOW: Virginia M. Month. 1940, 66, 33.

# OPHTHALMOLOGY, OTOLARYNGOLOGY

## THE USE OF HISTAMINE IN MÉNIÈRE'S DISEASE

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THE perfect treatment for Ménière's disease has not been announced nor will it be announced immediately. The story which I have to relate regarding its treatment with histamine is a simple one and can best be told as it actually happened. I do not wish to defend this method of treatment. It will survive or fall on its own merits.

### ORIGIN AND DEVELOPMENT OF TREATMENT

**CASE 1.** On August 5, 1939, a woman aged 44 years, was referred to me because of headaches. These headaches were most peculiar. For about 1 year, she had had attacks of left hemicrania in which the pain tended to extend to the occipital region and even down into the neck and shoulder. During an attack, marked tenderness of the temporal vessels and lacrimation of the left eye were noted. The application of an icebag to the head tended to relieve the pain, the application of heat exaggerated the pain. The attacks, although they sometimes occurred daily, had lasted for only a short time, frequently less than an hour. However, occasionally they had lasted for 24 hours or longer. She had noted that the ingestion of alcohol would precipitate an attack. The attacks invariably came on during the day and never at night. A typical attack was reproduced when the patient was given 0.48 milligram of histamine subcutaneously. The pain which was confined to the left side of the head corresponded to that which had been noted previously during spontaneous attacks. A diagnosis of "histaminic cephalgia" (erythromelalgia of the head) was made (5, 7).

"Desensitization" with histamine was started on the following day and within 15 days the patient was entirely free from headaches and stated that she felt fine.

This patient had had Ménière's disease for more than 4 years and she had been observed at the clinic at frequent intervals during this period, the histamine treatment instituted was not for Ménière's disease but only for the headaches. However, the headache, the tinnitus of the left ear, and the mild attacks of vertigo which she had been having from day to day, all disappeared. She felt that her hearing also improved. Furthermore, she stated that her head felt clear and the left ear was entirely free from the ringing noise for the first time in 4 years. She was much more elated over the fact that she was free from her vertigo and tinnitus than that she had been relieved of her headache. The heavy feeling back of the left ear disappeared and she was able to stoop over to tie her shoes, turn her head quickly from side to side, and to sleep without a pillow. She was

unable to do these things prior to this treatment. Incidentally, she had received ammonium chloride 3 to 4 times daily for the previous 4 years but this had not prevented the attacks of vertigo although it had greatly alleviated them. Subcutaneous injections of histamine were given twice daily for 63 days. During the first 15 days she received 2 injections daily, during the additional 48 days she received only 1 injection of 0.1 milligram daily and remained free from all symptoms of Ménière's disease.

Because of the favorable response to this treatment, 3 additional patients who had Ménière's disease were treated in a similar manner with good results. At a meeting of the Central Society for Clinical Research held in Chicago on November 3 and 4, 1939, H. L. Alexander and R. Elliott, of St. Louis, reported their observations on the treatment of chronic urticaria by means of the intravenous administration of histamine. They were of the opinion that this method was better than the subcutaneous administration of the drug. In view of the fact that I had already obtained good results in Ménière's disease with histamine administered subcutaneously, I felt that perhaps more prompt results might be obtained by the intravenous administration of the drug.

On November 6, 1939, C. H. Shelden and I (8) first treated a patient suffering from Ménière's disease by the intravenous administration of 19 milligrams of histamine acid phosphate<sup>1</sup> diluted in 250 cubic centimeters of physiological saline solution. The first patient so treated, who had been confined to bed for a period of 3 weeks because of Ménière's disease, was relieved promptly of all symptoms, was able to get up immediately after the injection was completed and walked about in a perfectly normal manner. This patient has apparently remained well. The first patient referred to in this paper who had been relieved of Ménière's disease by the subcutaneous administration of histamine again returned to the

<sup>1</sup>Presented before the Clinical Congress of the American College of Surgeons, Chicago, October 21-25, 1940.

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<sup>1</sup>In the course of this work histamine acid phosphate and histamine diphosphate have both been used. 1.88 mgm. of histamine acid phosphate or so called histamine monophosphate contains 1 mgm. of histamine base. 2.75 mgm. of histamine diphosphate contains 1 mgm. of histamine base.

clinic on February 19, 1940, because of a recurrence of acute Ménière's disease. She had not taken any histamine for 6 weeks preceding her second visit. On admission she had marked vertigo, nausea, vomiting and tinnitus which had been present for approximately 12 hours. We immediately started the intravenous injection of histamine. Within 30 minutes, she was free from nausea and vomiting and within 50 minutes the vertigo practically disappeared and the tinnitus was reduced to a marked extent. At the completion of the injection, she was able to get up and walk out of the room. The a severe acute attack of Ménière's disease which she had had in the previous 4 years had lasted approximately 2 weeks. She has remained well to the present (December 1940).

#### DIAGNOSTIC FEATURES IN MÉNIÈRE'S DISEASE.

In Ménière's syndrome vertigo is the essential feature and most probably represents a local process involving the labyrinth (8). The factor which is most likely responsible for the syndrome is local alteration in the permeability of the capillary wall resulting in local edema. Histamine is an important agent which affects capillary permeability. The resulting edema may well be comparable to the cotton-wool exudate in the retina and edema of the optic nerve head which are observed in malignant hypertension. Furthermore it is possible that progressive deafness without obvious cause may be the result of primary involvement of the cochlea. It is comparable to the situation which results when a person who has Ménière's syndrome has recurring attacks of severe vertigo, but without tinnitus or loss of hearing. The degree and extent of involvement of the labyrinth will determine the major presenting symptoms which are observed clinically. This hypothesis seems to be in keeping with the observations of Hallpike and his associates (2, 3, 4). The presence of tinnitus and varying degrees of deafness probably indicates that the process also involves the cochlea.

Caloric tests in determining vestibular function in cases of suspected Ménière's disease may be of some value but certainly are not necessary nor particularly significant in establishing a definite diagnosis. The range of functional activity in this group of cases encountered at the Mayo Clinic varied greatly. Slightly hyperactive reactions on one or both sides were observed in some cases and in others there appeared to be absolutely no response to stimulation. The average reaction would probably be considered to be normal or slightly on the hyperactive side. Most

of the caloric tests gave results within normal physiological limits.

I do not believe that diminution of hearing or deafness is necessary before a diagnosis of Ménière's disease is justified. A diagnosis of carcinoma of the stomach can be made in the absence of a palpable mass in the epigastrium and a diagnosis of thrombo-angitis obliterans in the absence of gangrene. By the same process of reasoning I feel that a diagnosis of Ménière's syndrome can be made even though the patient has no loss or even diminution in hearing. Loss of hearing like gangrene and a palpable mass, indicates advanced stages of the disease process.

#### METHOD AND RESULTS OF TREATMENT

Up to July, 1940 the intravenous injection of histamine had been used in 49 cases of Ménière's syndrome at the Mayo Clinic. Thirty-three of the patients were men and 16 were women. The ages ranged from 20 to 69 years for the men and from 28 to 59 years for the women. All had vertigo, 33 had tinnitus, and 38 had some diminution of hearing. All of the patients obtained prompt relief from vertigo, nausea and vomiting. Less than 50 per cent obtained improvement of tinnitus, the most difficult phase of Ménière's disease to treat. A small number reported improvement in hearing. Twenty-five of the 49 patients previously had undergone some type of Furstenberg treatment. Many of these had obtained palliative effect from this treatment, but the fact that they returned to the clinic for additional treatment indicated that they were not satisfied with the improvement. Some had received no benefit.

**CASE.** A man, aged 64 years, presented himself at the clinic for the second time on March 28, 1940, because of chronic progressive type of Ménière's disease. Symptoms had been present since 1916 and had been much more severe since August, 1938. At the time of his first visit in January, 1939, ammonium chloride plus low salt diet as advised. Later, he also was given large doses of potassium nitrate. Both forms of treatment failed, however. He slowly became one for the 14 months he received this type of treatment. He was unable to drive his car, could not move or turn his head quickly from side to side, or lean back and in chair as it would precipitate vertigo. Following two intravenous injections of milligrams each of histamine base in 5 cubic centimeters of normal saline solution, he was unable to bring on any of his previous symptoms. He was able to drive his car and resume his work. He remained entirely symptom free for 1 month. Since that time he has had occasional mild attacks of dizziness but is not in any way incapacitated.

Our method of treatment of Ménière's syndrome with histamine has not changed materially since Sheldon and I originally began this work.

The problem resolves itself, first into eradicating the acute symptoms of vertigo, nausea, vomiting and tinnitus, and this can be accomplished by giving 1 milligram of histamine base (2.75 mgm of histamine diphosphate) in 250 cubic centimeters of physiological saline solution. This solution is given intravenously at the rate of 50 to 60 drops per minute by the gravity method.<sup>1</sup> It usually requires 1½ hours to administer this amount of histamine. These intravenous injections can be repeated on successive days if the acute symptoms do not subside with the one injection. In acute Ménière's disease, it is usually impossible to give any type of medication by mouth because of the associated nausea and vomiting and yet these symptoms can, as a rule, be eradicated promptly by the intravenous administration of histamine. This is the chief advantage which histamine has over other types of therapy. Some patients seem to get along for months without additional treatment.

**CASE 3** A young man, aged 20 years, came to the clinic August 3, 1939, because of attacks of vertigo which he had been having for the previous 3 years. Except for these attacks, his health had been excellent. The attacks of vertigo apparently came on at any time regardless of what he happened to be doing. The onset was sudden and objects seemed to whirl counterclockwise. The severe attacks were accompanied by pallor, cold sweats, nausea, and vomiting. The minor attacks lasted only a few seconds and the more severe ones for half an hour or more. He had had deafness in the left ear as far back as he could remember, tinnitus was not present. He had been on a salt free diet prior to his admission to the clinic but had had no other type of medication.

General and neurological examinations gave essentially negative results except for complete nerve deafness on the left side. All routine laboratory studies, including a serologic test for syphilis and roentgenogram of the head, gave negative results. He was placed on the Furstenberg schedule and permitted to go home. He derived no benefit from this treatment and returned to the clinic on December 15, 1939, requesting surgical treatment for his condition. Instead, on December 16, 18, and 20, he received intravenous injections of histamine acid phosphate, the dose on each day consisted of 1.9 milligrams dissolved in 250 cubic centimeters of physiological saline solution. At the time of his dismissal from the clinic he was entirely free from vertigo. He had 1 recurrence 10½ months later. He was treated in a similar manner and is now well.

The second phase of the problem resolves itself into the prevention of future attacks. This phase of the work is still in progress, but I feel that an adequate maintenance dose of histamine given subcutaneously 2 to 4 times a week is the best procedure to employ. By an adequate maintenance dosage, we usually mean 0.1 to 0.2

milligram of histamine given subcutaneously 2 to 4 times a week.

**CASE 4.** A woman, aged 27 years, reported to the clinic November 20, 1939, because of attacks of dizziness and sensations of whirling which had occurred for 18 months. Nausea and vomiting invariably occurred with the sensations of whirling. She was often thrown to the ground during these attacks. Occasionally, she had as many as 4 attacks a day and was incapacitated because of these attacks. Some degree of vertigo had been present since the onset of her illness.

On November 25, 27, and 28, 1939, the patient received intravenous injections of 1.9 milligrams of histamine acid phosphate dissolved in 250 cubic centimeters of physiological saline solution. All of her symptoms disappeared but the symptoms recurred 3½ weeks later. She received 1.9 milligrams of histamine acid phosphate dissolved in 250 cubic centimeters of physiological saline solution intravenously on December 18 and again on December 19. She was entirely free from symptoms until February 2, 1940. Since that time she has received 0.1 milligram of histamine subcutaneously every other day and she has remained free from symptoms up to the present (approximately 8 months).

#### TINNITUS

For those who feel that surgical treatment is the only one to employ in Ménière's disease, Case 5 should be of unusual interest. A new method of recording tinnitus is described which should aid in lateralizing the disease and prevent the surgeon from cutting the wrong nerve. It represents a slight modification of the method Baldes and I (6) originally described for recording bruits. Tinnitus, as I have seen it clinically, is of two types. First is the high-pitched noise which patients usually describe as a sensation of escaping steam. If such a noise is identified in terms of frequency per second, it invariably proves to be high, usually of 500 or more vibrations per second. This type of tinnitus should be classified as primarily neurogenic in origin. If the vibrations were plotted, they would form a straight line. The second type is primarily vascular in origin and is synchronous with the heart beat. If the vibrations produced by the noise are plotted, they would form a wavy line. The second type of tinnitus is low-pitched and of less than 150 or even 100 vibrations per second.

**CASE 5** A man, aged 44 years, came to the clinic April 3, 1940, because of vertigo, nausea, vomiting, tinnitus and loss of hearing in the left ear of 4 years' duration. The tinnitus, which was subjectively confined to the left ear, had been present for 10 years. He had previously come to the clinic in September, 1939, with similar complaints. Just prior to his second admission, he visited two eminent neurosurgeons, both of whom advised surgical section of the left eighth nerve.

General and neurological examinations at the clinic gave negative results except for marked diminution in hearing of the left ear. The patient stated that he had two kinds of tinnitus in the left ear, one a constant, hissing sound

<sup>1</sup>Ampuls in two sizes are now on the market, one of which contains 2.75 milligrams of histamine diphosphate per cubic centimeter (1 mgm histamine base) and the other 0.275 mgm. of histamine diphosphate per cubic centimeter (0.1 mgm. histamine base).

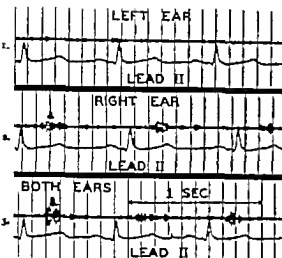


Fig. 1. Recording from left ear and simultaneous electrocardiogram illustrating lead II. N. bruit is present.

Fig. 2. Recording from right ear illustrating systolic bruit which occurs at simultaneously with the T wave in the accompanying electrocardiogram.

Fig. 3. Recording from both ears illustrating the same phenomenon observed in Fig. 2 when the recording was made from the right ear only.

which was high pitched and coarse rumbling sound which was synchronous with the heart beat. It localized both of these sounds in the left ear. During the time that histamine was being given intravenously the tinnitus which he heard in the left ear became pronounced. Two stethoscopes were connected so that the ear pieces of one were in the patient's ears and those of the other in the examiner's ears. It was easy to determine the origin of the tinnitus by alternately clamping the tubing from the patient's right and left ears. It was thus easy for the examiner to hear a bruit which originated from the patient's right ear. No bruit was heard from the patient's left ear. This bruit was accentuated with each systolic thrust. By means of selective sound amplifier, recording was made first from the left ear (Fig. 1) then from the right ear (Fig. 2) and finally from both ears (Fig. 3). Strange as it may seem, the bruit originated exclusively from the right ear although the patient thought the bruit originated from the left ear. Hearing was reduced in the left ear and normal in the right ear.

This patient had 5 intravenous injections of histamine base of 1 milligram each and then desensitizing injections

of histamine were given. He is still having transient attacks of vertigo at the time of his discharges which as on April 2, 1940. He continued to take 0.1 milligram of histamine base subcutaneously twice a day and on June 2, 1940, he reported that he was evidently well. I saw this patient November 27, 1940, at which time he stated that he was perfectly well.

#### OBSERVATIONS

At the time this paper was written, 15 of the 49 patients treated with histamine were known to be well. The others have had one or more recurrences of symptoms, possibly because they were not taking a maintenance dose of histamine. In a preliminary report of this type it is impossible to express results accurately in mathematical terms, but rather to express tendencies in terms of treatment. This work is still in progress and much remains to be learned concerning the pathological physiology in Ménière's syndrome but it is my impression that the ultimate treatment will prove to be medical, not surgical.

#### REFERENCES

1. FURSTENBERG, A. C. Ménière's symptom complex—medical treatment. *T. Pacific Coast Oto-Ophthalm. Soc.*, 1936, 50-60.
2. HALLPETER ET AL. Editorial: Ménière's disease. *Lancet*, 1940, 506-507.
3. HALLPETER, C. S., and CARRIS, H. Observations on the pathology of Ménière's syndrome. *J. Laryngol. & Otol.*, 1938, 53: 5-15.
4. HALLPETER, C. S., and WRIGHT, A. J. On the histological changes in the temporal bones of cases of Ménière's disease. *Proc. Roy. Soc. Med.*, 1939, 32: 446-455.
5. HORTON, B. T. Treatment of specific types of headaches with histamine. *J. Am. M. Ass.* (In press).
6. HORTON, B. T. and BALDER, E. J. A photographic method of recording bruit: means of differentiating aneurysm and arteriovenous fistula, preliminary report. *Proc. Staff Meet., Mayo Clin.*, 1937, 8: 5-824.
7. HORTON, B. T., MACLEAN, A. R. and CRABO, W. McK. A new syndrome of vascular headache: results of treatment with histamine: preliminary report. *Proc. Staff Meet. Mayo Clin.*, 1939, 14: 57-60.
8. SHELLEY, C. H. and HORTON, B. T. Treatment of Ménière's disease with histamine administered intravenously. *Proc. Staff Meet. Mayo Clin.*, 1940, 5: 7-21.

# THE SURGICAL TREATMENT OF MÉNIÈRE'S DISEASE

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MÉNIÈRE'S disease, or perhaps more correctly Mémère's syndrome, also less correctly known as aural vertigo, is characterized by a sharply defined group of signs and symptoms that is almost pathognomonic. It is one of the most common ailments referable to the cranial nerves. The symptomatic part of the syndrome is as follows: sudden and recurring attacks of dizziness in which objects rotate or oscillate, nausea, vomiting, and tinnitus. The objective part of the syndrome is partial deafness, the tinnitus is on the side of the reduced hearing. The two essential features of the syndrome are (1) dizzy spells, and (2) deafness. However, only rarely are the other symptoms—nausea, vomiting, and tinnitus—absent in at least some of the attacks. Ménière's disease may be unilateral or bilateral, the latter occurring in about 10 per cent of the total number. When bilateral the two sides may begin synchronously or independently.

Ménière's syndrome was established as a clinical entity by Ménière, a Frenchman, in 1861. He, however, knew nothing concerning its underlying cause, and in the search for a cause confused the clinical picture with that of a case of acute vestibulitis upon which a necropsy was performed. He found what is now recognized as a hemorrhagic purulent exudate throughout the semicircular canals. This, of course, was before the work of Pasteur, who established the bacterial origin of infection, and occurred during a period when hemorrhage was looked upon as the cause of sudden seizures, such as epilepsy. It was, therefore, not unnatural that the hemorrhagic content of the exudate should have been regarded as the cause of Ménière's disease—a concept which has thoroughly permeated the literature and is difficult to overcome even at the present time.

Ménière's disease is doubtless almost as old as the human race. Through descriptions of their characteristic seizures many prominent victims are known for several centuries back. It was in one of his numerous attacks that Martin Luther in an episode that has carried down through the centuries, threw the ink-well at the devil who was violently attacking his ear. Since the latter part of the eighteenth century attacks of this character have frequently been referred to as Dean Swift's

disease owing to the fact that this great satirist had so carefully described his own attacks. Throughout the latter half of his life the anticipation and realization of his frequently recurring seizures made him almost a recluse. Among medical men the great Hughlings Jackson was a noted victim. He wrote several articles on aural vertigo, his interest being largely stimulated by his own discomfort. Gamaliel Bradford, an American man of letters, so well known for his entertaining biographical sketches, was a victim of Ménière's disease in very virulent form. A vivid description of these attacks which he so aptly calls "the swoop of the hawk" was presented in his journal appearing in *Harper's Magazine* a few years ago.

Pseudo-Ménière's disease is Ménière's disease minus the deafness and tinnitus. In other words, there are the same recurring attacks (in which objects jump and rotate), but there is no indication of the side of the lesion. This condition is by no means uncommon. At times the unilateral features of Ménière's disease develop later. The frequent change from the pseudo-Ménière's to Ménière's disease with time means that in these cases the former is but an early stage of the latter. But that this metamorphosis does not always occur makes it necessary to retain pseudo-Ménière's as a distinct clinical entity.

**Symptomatology.** In some cases all of the cardinal symptoms of Ménière's disease—deafness, tinnitus, and dizziness—may occur almost synchronously. In other cases any one of the three may antedate the other two for weeks, months, or years. I have seen dizzy attacks grafted upon defective hearing or tinnitus of 20 years' standing. And in other instances after dizzy attacks have continued an equally long time, unilateral deafness and tinnitus have appeared. When dizzy attacks precede unilateral deafness or tinnitus, the diagnosis of pseudo-Ménière's disease must be made.

The dizziness of Ménière's disease (and pseudo-Ménière's) is of a very definite character—objects rotate or jump rapidly. Without dizziness of this type one cannot make the diagnosis of Ménière's disease. Patients who complain of general dizziness with a swooning sensation or an uncertain feeling in the head do not have Ménière's disease. The next essential feature of this dizziness is that it comes in recurring attacks. The onset is usually very sudden, at times so sudden and violent that

the patient is thrown to the floor and bones may be broken. The attacks last from a few seconds to many hours—even days. The patient must lie down at once and close the eyes but even then only a degree of relief is obtained. I have never known of a patient who could give any precipitating cause. In most instances, and in practically all in the beginning, the patient is perfectly well between attacks. In the later course of the disease there may be a more or less constant state of dizziness, always intensified by movements of the head. The direction of movement or rotation of objects during the attacks has not proved to be of any value in localizing the lesion to one or the other side, i.e. the objects may move in the same direction when the right or left nerve is involved.

*Tinnitus.* This is rarely absent and is, I think, just as definitely a localizing sign as the deafness. It may be intermittent or constant. It may be intensified before, during, or after an attack, but in perhaps the majority of the cases it is unchanged during the dizzy attacks. The tinnitus varies in its character—it may be a ringing, hissing or explosive noise. The beginning of tinnitus in the opposite ear is strong presumptive evidence that the syndrome is becoming bilateral.

*Deafness.* This is nearly always subtotal but in most instances—at least in the relatively late stages that we now see—the hearing is of little practical value. The audiometer curves are quite variable but in most instances all tones are more or less evenly affected. The deafness usually develops slowly and insidiously but it may appear fairly abruptly. It is usually progressive up to a certain point after which it is fairly stationary; however, it may steadily diminish until it is abolished. In about 10 per cent of the cases deafness is bilateral in the beginning or subsequently. Only occasionally is there improvement in the hearing once its downward course begins. At times the hearing disappears suddenly and as suddenly returns, but this is unusual.

*Nausea and vomiting.* In nearly all cases there is vomiting at some time. It may occur in a few attacks only—usually those that are most severe—or it may be a constant accompaniment. It may be continuous for days and be scarcely less severe than the dizziness. Nausea is much less constant and is usually more pronounced when the vomiting is severe.

*Other symptoms and signs.* Various other symptoms are not infrequently present. Diplopia is noted during the attacks in about one-fourth of the cases; no objective evidence of extra-ocular palsies can be observed at the time. Quite frequently patients have sensation of fullness or a

tight feeling in or about the affected ear. There may also be a sensation of a dull, heavy or even sharp pain which may radiate over the side of the head. I have even seen the pain referred down the arm and chest and from such a pain a diagnosis of angina has been made. It is quite possible that these are referred sympathetic pains. A tight feeling over the chest has been noted a few times. Headaches are not uncommon. They vary in location and severity: some are frontal others temporal, or occipital.

Following attacks patients may stagger. The staggering may or may not be to one side and if to one side it is just as frequently on the side opposite as on the side of the affected nerve.

Flashes of light, dark spots, rings, and dimness of vision may occur during and after the seizures. Momentary loss of consciousness occurs occasionally. A singular but constantly recurring complaint in one patient was an intense desire to urinate and defecate so that during the attacks the patient was forced to lie on a bedpan.

Lateral nystagmus, positive Romberg loss of corneal reflex on the corresponding side, a positive Babinski, and ankle clonus have been occasional objective findings. Such findings make one suspicious of an underlying tumor.

#### DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

If a patient has recurring attacks of dizziness in which objects whirl or move constantly the diagnosis is either Ménière's or pseudo-Ménière's disease; other signs and symptoms notwithstanding. If there is an additional partial deafness in *one* ear (and the deafness is not due to middle ear infection) the diagnosis is Ménière's disease. If in addition to the dizzy attacks there is partial deafness in both ears, the diagnosis is *bilateral* Ménière's disease. The only other lesion to be considered in the differential diagnosis is a tumor in the cerebellopontine angle and along the eighth nerve. From the 401 patients with Ménière's disease that I have operated upon there have been 3 tumors entirely unsuspected and all were very small. Usually patients who have tumors and Ménière's attacks at the same time show other signs that make the diagnosis of a tumor unmistakable. In the early stages of a tumor's growth and before contiguous structures are implicated, the differential diagnosis would be impossible for both tumors and Ménière's disease give identically the same objective findings, i.e. partial deafness in one ear. In going over the histories of acoustic and other tumors in the cerebellopontine angle quite a high percentage give the typical attacks of Ménière's disease. As a matter of fact the dif-

ferential diagnosis is not so important, for both lesions require the same operative exposure

#### ETIOLOGY AND PATHOLOGY

So far as I am aware, in only 2 cases of Ménière's disease has a study been made at necropsy. These were by Cairns, of London, who because of certain histological findings concluded that the cause was in the semicircular canals. This deduction is by no means secure and I think is very doubtful. There is a certain amount of pathological material available from the operative exposures, but since there is no gross lesion in two-thirds of the cases, some doubt remains that one interprets correctly the finding in the minority of cases. That there is an organic lesion is, of course, evident at once from the omnipresent deafness. And deafness is referable to the auditory branch of the eighth nerve and is not responsible for the dizziness, which must be referable to the vestibular branch of this nerve or possibly its end organ—the semicircular canals. Since both the vestibular and cochlear divisions of this nerve are involved, it is evident that the lesion is in the nerve itself and not the end organ—a lesion affecting both the cochlear and the semicircular canals, which are quite a distance apart, would be highly unlikely. It is this fact that causes one to doubt Cairns' conclusion that the lesion is in the semicircular canals. Another reason for assuming that the causative lesion must be in the nerve and not in the end organs is that the attacks are paroxysmal. Unquestionably Ménière's disease is similar in this respect to trigeminal neuralgia and epilepsy. There can now, I think, be no doubt that *only* a cerebral lesion can cause epilepsy, and there can scarcely be a doubt that trigeminal neuralgia is due to a lesion in or on the sensory root, i. e., in both instances a higher neurone, and never a peripheral nerve or end organ, is the site of the lesion causing paroxysmal attacks. A peripheral lesion cannot cause recurring paroxysmal attacks. Operations upon the sensory root of the trigeminus through the posterior fossa disclose a gross lesion in the root in a high percentage of cases—75 to 80 per cent. The lesions are of different kinds—tumors, aneurisms, congenital malformations, and arteries compressing the bare nerve. Similar lesions have been found in Ménière's disease, though in a much smaller percentage of cases—about 35 per cent. In the remaining cases there is unquestionably an intrinsic change in the nerve. From several small pieces of nerve removed at operation there appears to be an increased fibrosis, occurring irregularly and doubtless replacing areas of degeneration in the nerve.

On the other hand, infections that attack the middle ear are probably never followed by Ménière's disease. In the occasional cases in which the semicircular canals (vestibulitis) are directly affected during the extension of a mastoid infection, the dizziness is continuous and gradually abates. I have not seen the recurring attacks of Ménière's disease following the recovery of vestibulitis.

From the negative side it is worthy of note that if Ménière's disease were the result of infections of the middle ear and mastoid sinuses, it would be particularly prevalent in childhood when these infections are so common and when Ménière's disease is almost unknown. Nor is there the slightest evidence to support the thought that focal or systemic infections are directly or indirectly responsible for Ménière's disease. I have never seen an instance of Ménière's disease in which syphilis, tuberculosis, or other chronic inflammatory process was found to be responsible for Ménière's disease, and this despite the fact that bilateral deafness is such a well recognized sequel of syphilis.

Ménière's disease is almost exclusively a disease of middle or more advanced age. This favors its production from thickening of the arteries along the nerves.

For reasons unknown the *left* auditory nerve is the site of these Ménière's attacks about twice as frequently as the right. There is little, if any, difference between males and females.

#### SURGICAL TREATMENT

Ménière's disease can be permanently cured by division of the auditory nerve. This procedure carries almost no risk to life. Up to the present time I have performed 401 operations, with 1 death—the 358th case—due to meningitis.

Total division of the auditory nerve destroys the remaining hearing in that ear, but that is usually of little practical significance. However, at times it may be important to preserve it, especially when the hearing in the opposite ear is also defective or when the patient's position is dependent upon the preservation of some hearing in both ears, as in certain positions on the railroad. In recent years partial division of the eighth nerve has been used when there is reason to save the remaining hearing. The vestibular branch of the nerve can be divided leaving the auditory branch, and consequently the hearing, intact. There is only rarely a line of division between the two branches of this nerve so that a mathematical division of the nerve is necessary. Usually three-fourths of the anterior part of the nerve is sectioned in order to insure total elimination of vestibular fibers. It has been found that division of



even three fourths of the auditory division of the nerve does not affect hearing (because of redundant fibers carrying similar functions) and this permits a good margin of safety in insuring destruction of all vestibular fibers that may be included with the auditory fibers. Even so, fractional division of the nerve is attended by a fair percentage (10 per cent to date) of recurrence because the vestibular fibers extend even farther than the line of section. If a patient has bilateral Ménière's or pseudo-Ménière's disease, it is necessary that fractional division be performed on both sides in order to preserve the remaining defective hearing in the one condition, or the normal hearing in the other.

#### THE OPERATION

Section of the auditory nerve can be done almost painlessly under local anesthesia. There is no sensation when the nerve is sectioned. After the scalp has been procainized the only remaining sensitive area is the under surface of the cerebellum but by gentle traction the pain is very slight. However avertin anesthesia is so perfect that I use this almost exclusively. A vertical incision is made along the mastoid and at the tip the incision is curved medially and downward to a point even with the occipital nerve which can usually be spared. Only a small cut is made through the insertion of the trapezius muscle. The flap of muscle and skin is reflected medially and then a small circular or oval area of bone is removed with the rongeurs. The bony defect, about the size of a 50 cent piece, is carried laterally as far as the mastoid cells but not into them. If, as occasionally happens, one is opened it should be immediately sealed with wax. After the dura has been opened, the cisterna magna is exposed by retracting the cerebellum and its contents evacuated by tearing a small opening in the leptomeningeal wall. This necessary procedure provides ample room and permits easy retraction of the cerebellum without trauma. The cisterna lateralis is then opened and the contained fluid is aspirated through a suction tube. The eighth nerve then stands in full view. A small hook is gently passed around the nerve which is elevated, thus exposing the concealed seventh nerve. The handle of the hook is then touched with the electrocautery and the nerve is instantly severed. If partial section of the nerve is desired the hook passes under the anterior border of the nerve to the desired point of division and the cautery is applied in the same manner. At times vessels—arteries or veins—in the meninges or even directly on the nerve must be coagulated and divided or pushed aside before the

nerve can be safely divided. The facial nerve can, but should not, be injured if the auditory nerve is carefully retracted before its division.

In closing it is important that the dura be carefully sutured, otherwise intracerebellar hemorrhage might occur from the trauma that results from the thrust of the cerebellum against the edges of the bony opening during vomiting or coughing. Then, too, it is safer to exclude any danger of a cerebrospinal fistula. If the dura is defective a pedunculated or a free muscle transplant (from the under surface of the trapezius) is sutured to the dural margin. When carefully and properly done the procedure is almost without risk.

#### AFTER EFFECTS OF DIVIDING THE VESTIBULAR NERVE OR NERVES

If one auditory nerve—or only its vestibular division—is divided there is no permanent loss of vestibular function of any kind. Immediately after the operation the patient may or may not have transient, even severe dizziness, not unlike a Ménière's attack. When this occurs it usually disappears in a few days. However there may or may not be dizziness on turning the head for a period of days, weeks, or even months. This, too, always gradually lessens and eventually disappears entirely. Only occasionally does this disturbance continue for any length of time.

Tinnitus may or may not disappear after the nerve is sectioned, and if it persists it may or may not be improved. In about 50 per cent of the cases it disappears completely. One can assure patients that they will never have another attack of dizziness after section of the nerve, if the syndrome is unilateral but no promise can be made concerning the tinnitus, which a sensible person learns to disregard. There is no staggering gait, and a perfectly negative Romberg after section of one nerve.

Division of both vestibular nerves is attended by one rather surprising after-effect, i.e. jumbling of objects (visual) when the patient is in motion as soon as the patient is at rest the objects are again perfectly clear. The other disturbance is uncertainty when the patient is walking in the dark. Both of these persist, though with gradual lessening in severity. But both are gladly borne for the relief of the dizzy spells which are no longer possible. These two disturbances indicate the very intimate association between the vestibular and the visual apparatus in human beings. In this connection it is interesting to note that not infrequently during Ménière's attacks and after section of one or both eighth nerves, there is transient diplopia.

Perhaps most surprising is the fact that after both vestibular nerves are sectioned, the gait is normal and the Romberg negative. Doubtless in human beings the cerebellum almost entirely controls this function and has less important dependence upon the semicircular canals, this is not true in animals, to whom the semicircular canals are so important that when eliminated it is impossible to stand or navigate. It is also important to note that when both auditory nerves are sectioned in bilateral Ménière's disease the tinnitus may or may not persist, exactly as with the unilateral type.

Concerning the two types of medical treatment that have been introduced in the past few years,

I can only say that very few patients whom I have operated upon in recent years have not tried either or both of them without success. The syndrome is one that lends itself quite well for a time to statistical conclusions because of the marked variations in the frequency of attacks. Some patients will go for months or even years between attacks and what is done last gets the credit for the free interval—*post hoc ergo propter hoc*. I must say that there is nothing in either type of medical treatment but I certainly do believe them to be useless, and I do know that operation cures the disease with almost no risk and with no after-effects.

## MEDICAL TREATMENT OF MÉNIÈRE'S DISEASE

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SINCE Ménière, in 1861, first described a disease characterized by recurring attacks of vertigo and unilateral deafness associated with a pathological condition of the inner ear, the exact nature of which is presumed to have been hemorrhage, the eponym has remained in the literature as Ménière's disease. His distinctive contribution was the recognition of the fact that vertigo, nausea, vomiting, deafness, pallor, sweating, and occasional loss of consciousness are due to a lesion in the peripheral vestibular organ and not, as was then held, to a cerebral crisis. Fortunately, Ménière was able to demonstrate a lesion in the labyrinth of a young woman who had died on the fifth day after the onset of these symptoms, although death was probably not caused by the lesion. Ménière also called attention to a tendency for these attacks to recur and to be accompanied by unilateral deafness.

Since that time many reports of similar occurrences have appeared in the literature, until it has been recognized that all cases are not cut to the same pattern, the attacks of vertigo varying in degree of severity and in periodicity of recurrence. Nausea, vomiting, and tinnitus are not always present and vary greatly in degree. For this reason there has arisen a tendency to differentiate the milder attacks which occur without all the recognized symptoms from the disease as originally described, under various pseudonyms, such as Ménière's syndrome, Ménière's symptom

complex, paroxysmal vertigo, and recurrent vertigo.

Northington has put forward a number of cogent reasons for omitting the eponym and has classified the varied manifestations under "peripheral vestibular syndromes," Ménière's disease being recognized as "recurrent vestibular symptoms of obscure or unknown origin." He also points out that the eponym presupposes a condition without any proved pathology and therefore discourages any serious search for a possible etiology. It has been emphasized many times, however, that the condition is not a disease entity in itself but rather a combination of symptoms which may occur with several widely separated lesions, such as pressure on or neuritis of the auditory vestibular apparatus, brain tumors, cardiovascular condition, infectious foci, syphilis, allergy, and so forth.

At the present time, then, it would seem that by the doctrine of good use, the term "Ménière's disease" has come to mean a sequence of signs and symptoms referable to the peripheral vestibular apparatus but without any demonstrable pathology of this organ. Crowe considers that the presence of recurring vertigo alone, without deafness or tinnitus, is sufficient evidence upon which to base the diagnosis.

It seems unnecessary to note any particular violence or frequency of the attacks before the diagnosis is made because every patient complaining of recurrent vertigo should be considered a potential victim of the disease. In this way we

may be able to answer Dandy's query as to whether or not it will be possible to diagnose the condition early in its course and thus conserve hearing in those who have not suffered any previous loss.

#### PATHOLOGY

While the pathology of the disease is unknown, the symptoms resemble so closely those arising from a stimulation of the labyrinth by the usual tests and an irritation or destruction by inflammatory disease as to suggest that the peripheral end organs rather than the central ones are at fault. Crowe cites the following reasons, among others, for suspecting the peripheral system: the vestibular symptoms differ only in intensity from functional tests; the infrequency of vestibular symptoms arising from intracranial tumors argues against the disease being in the nerve or the central vestibular nuclei; involvement of other cranial nerves is very rare; choked disc is not present; trauma of the vestibular nerve does not cause symptoms; no pathology has been found in nerves sectioned for study; the strongest reasons for suspecting pressure and chemical changes are the frequency and length of the remissions.

Brunner has contributed an interesting study of the present status of Ménière's syndrome. From an analysis of his own cases of Paget's disease as well as the cases of Hallpike and Cairns and others he concludes that the Ménière's attack corresponds to an attack of otitis interna vasomotoria.

#### SYMPTOMS

**Vertigo.** The vertigo of Ménière's disease is characterized by the suddenness of its onset at any time of the day or night, and even during sleep. The violence of the attacks may vary from a slight giddiness to an overpowering vertigo, which immediately incapacitates the subject and may be accompanied by nausea, vomiting, pallor, sweating, diarrhea, and collapse; these symptoms continuing for a varying length of time from minutes to days. If the patient is observed during the attack there is invariably seen a horizontal or rotary nystagmus, the quick component of which may be in either direction but is usually to the healthy side. Owing to the irregularity and short duration of many of the attacks, this symptom is rarely observed.

**Deafness.** A constant impairment of hearing on one side is always present at some stage of the disease. Cases have been reported in which loss of hearing was not demonstrated until number

of attacks had occurred. It is a not infrequent experience to find that a unilateral deafness has been present for years, either unknown to or forgotten by the patient, however increased deafness is usually evident at the time of the attack.

**Tinnitus.** This is a variable symptom. It is often prodromal and is usually unilateral. If bilateral it is more pronounced on the side of the greater deafness. Dandy states that in the presence of bilateral deafness an increase of the tinnitus on one side during a seizure is a definite aid in determining on which side the lesion is to be found.

**Labyrinthine tests.** It is obviously very difficult to obtain adequate results from these tests during a severe attack. Between seizures the caloric reactions may be normal but are usually somewhat diminished and at times markedly decreased. It is important to realize that whatever the grade of the reactions obtained, they must fall into the normal pattern; any perversion of this pattern must be regarded as indicative of a possible intracranial lesion.

The patient's description of the dizziness is often so indefinite that a comparison of the sensations obtained by the caloric test with that from which the patient suffers is frequently of value in establishing the diagnosis.

#### DIFFERENTIAL DIAGNOSIS

It seems necessary to discuss only one disease in the differential diagnosis on account of the serious nature of the results which ensue when it is not recognized. The symptoms of an acoustic neuroma in the early stages may strongly resemble Ménière's disease. In that the vertigo and dizziness are of the recurrent type and deafness occurs early. The vertigo, however, is rarely so sudden in onset or so severe in degree as is the case in Ménière's disease; the deafness, however, is of the same type in both conditions. The labyrinthine tests are sometimes of use in the differential diagnosis. Marked or complete loss of all reactions to the caloric test on one side, together with a loss of reactions from the vertical canals on the opposite side while not pathognomonic, strongly suggests the presence of a sub-tentorial lesion in the region of the cerebello-pontine angle. Later the development of signs of intracranial pressure and of involvement of other nerves serves to establish the diagnosis of an intracranial tumor.

#### MEDICAL TREATMENT

The literature attests the effectiveness of many methods of treatment, which suggests not only

that the pathology is unknown but also that its causes are variable. Attacks may be so infrequent or vary so in intensity that one applies some method of treatment deemed successful, only to have the symptoms recur with increased frequency and violence. In these circumstances it might be well to adopt the rule used in judging cancer cures, "the five year rule."

To facilitate the discussion of treatment, it is advisable to classify the disease according to its etiological factors. These types are as follows: systemic disease, toxic labyrinthitis, a term in common use among otologists; mechanical type, non-inflammatory lesions of the middle ear, apoplectic type, hemorrhagic and traumatic, Ménière's disease of obscure or unknown origin.

**Systemic disease.** Symptoms of Ménière's disease may occur in conjunction with some systemic disease, the recognition and correction of which will relieve the distressing symptoms. Northington cites a case with diabetes as the exciting cause, in which relief was obtained by diabetic treatment. Changes in the blood supply to either labyrinth, developing either suddenly or slowly, may upset the equilibrium between the two and cause a considerable disturbance. Sudden anemia or hyperemia brought on by vasomotor disturbances are a not infrequent etiological factor.

Endocrine disturbances may at times have some influence. One case emphasizes the importance of the "five year rule." M. D., suffering from a typical Ménière's syndrome, was found to have a low basal metabolism for which thyroid extract was administered with complete relief of the vertigo for 4 years, at the end of which time the symptoms returned with increased severity. A trial of a low salt diet and ingestion of ammonium chloride proving unsuccessful, complete relief was obtained by section of the nerve.

**Vitamins.** Avitaminosis as an etiological factor in deafness has been the subject of numerous studies and communications during the last decade. It is not surprising, then, to find that avitaminosis has been identified as a cause of Ménière's disease. Morch and Adams have cited several cases of the disease occurring with a very evident lack of vitamins, in particular vitamin C.

A comprehensive review by Dean before the American Otological Society in 1937 leaves no doubt that allergic diseases of the ear may cause a typical Ménière's syndrome, although the hearing, which is diminished at the time, usually returns to normal.

Treatment of psychosis at times plays a part in lessening the frequency of attacks. S. C. H., 70 years old, had suffered from Ménière's disease 10

years previously but had been free of attacks for 7 years. There was a marked residual deafness on the right side. One year previously the symptoms returned with marked loss of hearing on the left side. Some relief was obtained from a salt free diet and ammonium chloride, but the constant presence of a male nurse by allaying the patient's anxiety did more to reduce the number of attacks. Again, during the bank crisis of 1929 and the ensuing depression many patients presented themselves complaining of dizziness and vertigo which, no doubt, were due to nervous fatigue and an anxiety neurosis.

**Toxic labyrinthitis.** Foci of infection in relation to Ménière's syndrome have been demonstrated frequently, and otologists as a rule classify this type of Ménière's disease as toxic labyrinthitis. Many cases can be cited in which relief from the symptoms has been obtained by the clearing up of some focus, whether in the sinuses, tonsils, teeth, prostate, or gastro-intestinal tract. Here again it must be emphasized that deafness is a variable factor. Loss of hearing, a sense of fullness, and a buzzing sound in the ear is a usual complaint but is not invariably present at the time of the attack and may occur some time after it. Deafness, if present during the attack, tends to return to normal after the cessation of the symptoms.

Wright has eradicated all foci of infections he could reach in 23 patients. The vertigo was cured in all 23 and in 13 hearing returned to normal.

**Mechanical type.** Local disease in the middle ear has been shown to cause the symptoms of Ménière's disease. Acute and subacute closure of the eustachian tube has at times been identified as an etiological factor, and inflation of the middle ear is considered by Mygind and Dederding to be an essential part of the treatment. Vertigo and deafness may be brought on by a thin, relaxed, and greatly retracted drum membrane, particularly when the area of greatest retraction is about the incudostapedial joint.

A. N. had suffered from deafness and vertigo for several years, and this had persisted in spite of varied treatments. The drum membrane was found to be draped over the incudostapedial joint, and pressure over this area caused immediate vertigo. The application of a paper splint to the area resulted not only in relief from the vertigo but in marked improvement in the hearing.

**Apoplectic type.** This type of Ménière's disease is characterized by a loss of consciousness during the initial or subsequent attacks. Ménière's first contributions were his efforts to prove the syndrome to be due to some disturbance of the

labyrinth rather than to a "cerebral crisis," as had been held up to that time. Fortunately he was able to demonstrate a definite lesion in one of his patients at postmortem examination 5 days after the onset of the initial symptoms. Since then very few complete pathological studies of the labyrinth in this disease were made prior to the report of Hallpike and Cairns in 1938. Politzer apparently considered the apoplectic form of the disease to be always due to hemorrhage. He says

"Ménière's disease presents itself either with symptoms of an apoplectic form of congestion of the brain, or in the form of true apoplectic attack. It begins with dizziness, tinnitus, noises or roaring, staggering gait, and marked deafness, or the individual falls suddenly with loss of consciousness as if struck down. Consciousness usually returns after short time.

Treatment of this type is of little avail. Rest and sedatives until the acute reaction has subsided are indicated, and as the opposite labyrinth becomes accommodated all sensations of unsteadiness disappear. The resulting deafness is always very marked or complete, and the semicircular canals fail to respond to stimulation.

*Ménière's disease of obscure or unknown origin.* The more recent studies of Ménière's disease have stressed the importance of water and mineral metabolism, from which has arisen the theory of retention as an etiological factor. Throughout the literature frequent reference is made to the sudden changes in labyrinthine pressure, either hypertension or hypotension leading to a corresponding hyperemia or anemia. Only in this way can the tendency of the attacks to recur be explained.

Renewed interest in the medical treatment of Ménière's disease has been stimulated by the researches of Mygind and Dederding, who believe that the symptoms are due to increased pressure in the semicircular canals and attribute this increase to a faulty water metabolism which allows water to collect within the cells, resulting in subcutaneous infiltrations and overloading of the fluid in the labyrinth. The variability of the symptoms is explained by the varying amount of retention of the fluids in a predisposed labyrinth, in particular these investigators stress the rapid variations in the ability to learn, which is dependent upon the amount of water retention. They believe that this is a vasomotor phenomenon from which arises vascular and especially a capillary dysfunction. Their patients suffer from a peripheral disturbance of the circulation as manifested by chilly sensations, cold hands and feet, vasomotor rhinitis, phenomena which come and go in periods exactly corresponding to the aural phenomena, particularly deafness.

"We maintain, they conclude, 'that but we here have to deal with in the subcutaneous infiltrates, in the ear of the Ménière patient, and probably in other parts of the organism, is an edema contingent on defective function of the vessels, in particular defective function of the capillaries, an edema which, in number of important points, distinctly differs from nephritic and cardiac intercellular edema. We have believed that in our patients it was an intracellular edema caused by water leaking out through the enlarged stomata of the dilated peritubular capillary all.

Treatment is directed toward a reduction of the edema by diminishing the fluid intake and by a salt free diet, and also by various physiotherapeutic measures.

These principles are in agreement with the earlier writings of Földes, who in *A New Approach to Dietetic Therapy* attempts to show that disturbances of the water and mineral metabolism are important pathogenetic factors in a number of diseases, including epilepsy migraine bronchial asthma, allergic diseases and hypertension, in 1935 Ménière's disease was added to the list. Földes contends that water and mineral retention may be present without signs of edema, and, moreover without apparent cause. Two kinds of disturbance of the water and mineral metabolism are particularly met with in these diseases "general retention of water and minerals, and mobilization and consecutive local accumulation of water and minerals previously retained through the body." Both retention and sudden mobilization and elimination of retained water and minerals give rise to symptoms, and the treatment, being directed against retention, militates against any sudden mobilization.

In his statement of general principles Földes says

All pathological conditions discussed in this book are distinguished by two peculiarities (1) that although they present themselves as different phenomena, they are manifestations of one occurrence common to all, (2) the accumulation of water and minerals in one organ or the other in the entire organism, and (3) that, although besides retention, various other factors are necessary to the development of the respective disturbances (social disposition, endocrine constellation, etc.), the accumulation of water and (or) minerals is condition sine qua non.

The general principles of treatment are largely dietary. Use is made of the diuretic effect of a high protein, low carbohydrate and low fat diet, since the last two when given in normal or increased quantities are considered to favor retention of water and mineral salts.

Földes does not consider a restriction of sodium chloride either feasible or necessary. He holds that salt is not retained if the intake of liquids is restricted but has a diuretic action. Therefore the only limitation in his diet consists of an

avoidance of distinctly salty foods and of an excess of salt with meals. The amount of liquids to be ingested is limited to about 1 liter, including the fluid content of fruits. The caloric value of the diet is necessarily low, owing to the restriction of carbohydrates and fats. The use of diuretic drugs is not feasible, physical exercise and massage are of value.

Furstenberg, Lashmet, and Lathrop have questioned the accuracy with which the water exchange was measured by Dederding and his associates, and in studies of their own have arrived at the conclusion that the attacks of vertigo occur quite independently of whether water is retained or lost by the body. Furthermore, they found that attacks were produced by the administration of sodium, regardless of whether this was attended by hydration or dehydration. The therapeutic indications are, therefore, to permit as small an intake of sodium as is possible by means of a salt free diet, and to prevent the accumulation of sodium in the body by the administration of acid-producing salts such as ammonium chloride. These investigators report the successful treatment of 14 typical cases of Ménière's disease by this method, all the results being identical. In every case an attack could be precipitated by the administration of sodium chloride. In a later personal communication to Crowe (1937), he says that 125 patients had been treated by this method with splendid results. However, he found it necessary to hospitalize them because of the difficulty in controlling the diet, and because patients are prone to take medicines containing sodium. In 1 case he found that the water supply contained 30 grains of sodium per liter.

The successful results reported by Mygind and Dederding and by Furstenberg attest to value of this treatment. Furthermore the differences in the regimens can be regulated easily, since they occur in the more readily adjustable factors, namely the amount of water intake and the medication.

Finally, a much simpler form of treatment, in our experience over the last year, has proved fully as successful as any heretofore undertaken. Talbott and Brown, recognizing that the regimens of Mygind and Dederding and of Furstenberg were therapeutically successful in spite of their divergent views as to the actual mechanism, became interested in the concentration of electrolytes and the degree of hydration of the blood, both before and after treatment, since neither of these factors had been studied. Their second interest in the study of the blood constituents was particularly the level of the serum potassium. They point out

that in a disturbance of conduction of nerve impulses, such as in familial periodic paralysis, a change in concentration of serum potassium is observed and assert that the proper treatment is a high potassium intake. Similarly, symptoms of myasthenia gravis are relieved by a high potassium diet.

In a study of 48 patients suffering from Ménière's disease, the constituents of the blood failed to show any consistent changes from the normal. Furthermore, Talbott and Brown were unable to induce acute attacks in 4 patients by the administration of water or sodium salts. They concluded, therefore, that the therapeutic effect was not achieved by alteration of the concentration of sodium and water in the serum. A further study of the low sodium diet suggested a possible alteration in the proportion of sodium to potassium and if a low sodium diet with a normal potassium content was therapeutically effective, it seemed to them reasonable to try a diet proportionately higher in potassium. To achieve this result, from 6 to 10 grams of potassium chloride in an aqueous solution is given daily, and no other dietary modifications are advised.

Talbott and Brown conclude

"In a study of 48 patients with Ménière's syndrome, the concentrations of the acid base constituents of the serum were determined one or more times on 28 patients. The constituents included total fixed base, sodium, potassium, calcium, chloride, total carbon dioxide, phosphate, protein, and non protein nitrogen. Some bloods were drawn during acute symptoms, others were drawn when patients were relatively symptom free. No constant variation from normal in the concentration of constituents was observed. Four bloods, however, which were taken during an acute attack showed an increased concentration of serum potassium and a decreased concentration of serum sodium.

"An attempt was made in 4 cases to induce an acute attack. Large amounts of sodium salts were given intravenously and orally in order to produce an increase in concentration of serum sodium. This increase was accomplished in each case without any exacerbation of symptoms. It was concluded that neither hydration nor alkalosis nor an elevated serum sodium is a necessary accompaniment of acute symptoms of Ménière's syndrome.

"The therapeutic effect of this regime has been reassuring. It cannot be considered as a cure for all the symptoms, but clinical improvement has been impressive."

The potassium chloride is administered in a 25 per cent watery solution, each dram containing 1 gram of the salt. The salt is usually well borne, but an occasional patient complains of some distress. Potassium gluconate is tolerated well in larger doses than is potassium chloride and is now readily obtainable.

The precise action of potassium chloride on patients suffering from this disease is not known. Probably the diuretic action of the salt is an im-

portant factor in hastening the excretion of water and sodium chloride. Talbott and Brown believe that "there is a gradual accumulation of evidence which supports the suggestion that the conduction of the nerve impulses is probably associated with an optimal concentration of potassium in the surrounding medium. Any alteration of this concentration may upset a delicate mechanism.

It is apparent that studies in water and mineral metabolism have yielded definite results and still offer a fertile field for investigation. Developments in our knowledge of the vitamins also show promise of increasing usefulness in the treatment of Ménière's disease.

# BIBLIOGRAPHY

- ADAMS, J. Ménière's syndrome and vitaminosis. *J Laryngol. & Otol* 93, 54, 76
2. BROWN, MADELAINE R. The medical treatment of Ménière syndrome. *J Am. M. Ass* 937, 68, 58
3. BRUNNER, H. *Laryngoscope*, 93, 49, 77-908
4. CANNON, R., and F. COTT, M. S. Fluid balance in Ménière's disease. *Lancet*, 934, 1204.
5. CROW, S. J. Ménière's disease: study based on examination before and after intra-tympanic division of the vestibular nerve. *Medicine*, 913, 7
6. DAVIS, W. E. Ménière's disease—symptoms, objective findings and treatment in forty-five cases. *Arch. Otolaryngol.*, 934, 30
7. DZIMBOWSKI, DINA. Clinical and experimental examinations in patients suffering from M. S. Ménière. *Acta oto-laryngol.*, 934,
8. Idem. Our Ménière's treatment. *Acta oto-laryngol* 934, 6, 404
9. FOLDES, L. A New Approach to Diabetic Therapy. Boston: Richard C. Badger, 932.
10. Idem. A new concept of Ménière's disease and its response to antireflexion therapy. *Am J Digest Dis* 935, 243.
- FUERNBERG, A. C., LAURENCE, F. H. and LATANOW, FRANK. Ménière symptom complex; medical treatment. *Ann. Otol. Rhinol. & Laryngol.*, 934, 43, 35.
- HALLPIKE, C. S. and CURRIE, H. Observation on the pathology of Ménière's syndrome. *Proc. Roy. Soc. Med* 935, 3, 317.
3. MÉNIÈRE, M. P. Maladie de l'oreille interne offusquée, les symptômes de la congestion orbitale apoplectiforme. *Gaz. méd. de Par* 3d series, Feb. 9, April 5, June 5, Sept. 50
4. MOORE, P. Traitement de la maladie de Ménière et d'autres affections s'accompagnant de bourdonnements otogènes et de vertiges par les stambers. *Acta oto-laryngol* 930, 25, 620-637
5. MORGAN, R. H. Hypertension auris interna hiberniensis. *T. Dublin Oto-Laryngol. Soc., Hosp. Tid* 934, 70, p. 56
16. MORGAN, S. H. and DZIMBOWSKI, DINA. The significance of water metabolism in general pathology as demonstrated by experiments on the ear. *Acta oto-laryngol* 934, 7, 434.
7. Idem. Ménière's disease—II. Clinical experiments with reference to the influence of the water metabolism on the ear. *Ann. Otol., Rhinol. & Laryngol* 934, 47, 360
8. Idem. Ménière disease—III. The diagnosis and treatment of Ménière's disease. *Ann. Otol. Rhinol. & Laryngol* 934, 47, 766.
9. NORTHINGTON, PAGE. The diseases of the vestibular system. Nelson Loose Leaf Medicine of the Ear. Edited by Edmund P. Fowler. New York and Edinburgh. Thomas Nelson & Sons, 930.
20. WILKINSON, A. J. *J Laryngol. & Otol* 934, 53, 97

# PRIMARY CARE OF INJURIES OF THE FACE AND JAWS

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**I**NJURIES to the face and jaws vary widely in severity. They may be limited to the most superficial cuts, scrapes, or bruises of the soft tissues. Such wounds, although not serious in themselves, may result in conspicuous scars or deformities when improperly treated.

The more serious injuries are those causing deep, penetrating wounds, or involving fractures of the facial bones. They assume added importance for two reasons: (1) serious complications may develop from a fracture in close proximity to the cranium, (2) gross depressions or deformities even more noticeable than superficial scars may result from injury to the framework, the bone or cartilage of the face.

The result of any such injury may be the cause for much mental distress. The victim of an injury to the face may be permanently hampered by a conviction of unsightliness, whether fancied or real. One cannot overemphasize, therefore, the importance of early adequate treatment of these wounds, whether mild or severe, as the greatest safeguard against serious complications and subsequent deformities. This first aid care can best be given in the hospital. Facilities are generally available to transfer injured patients without loss of time to the accident ward, and therefore in this discussion we will place ourselves in the emergency ward when the accident victim is brought in, bleeding from the nose, mouth, or ears and with lacerations of the face. Obviously, after a hasty examination, the first duty of the surgeon is to control bleeding. Although patients may lose a considerable amount of blood on the way, primary hemorrhage from a cut about the face seldom leads to serious complications. Most lacerations stop bleeding spontaneously under continued pressure maintained with a sterile dressing. However, profuse hemorrhage through the nose from either the septal or the nasopalatine arteries, may be more serious. The procedure in this case is to clean out the blood clot from the nasal passages and pack with sterile gauze saturated with a solution of adrenalin chloride 1:1000. If this is not sufficient, postnasal packing should be resorted to.

After the bleeding is controlled, the surgeon has a better opportunity to examine the patient

carefully and make plans for further treatment. Of primary importance is an evaluation of the patient's general physical condition. In certain cases it is best to postpone immediate operation. If the patient obviously is in shock or has lost a large amount of blood, operation should be postponed until transfusion or intravenous fluids have decreased the risk from further surgical trauma. In every serious injury, particularly of the upper half of the face, we must keep in mind the possibility of a cranial injury, and if there are any symptoms pointing in that direction, consultation with a neurosurgeon is indicated.

Bleeding from the nose may be due to a fracture involving the cribriform plate, this may eventually cause leakage of cerebrospinal fluid through the nose. When the latter is mixed with blood it may escape detection. Bleeding from the ears may be due to simple laceration of the tissues of the ear canal, which is not serious, or it may be due to a fracture of the parietal or temporal bones. If there is evidence of brain injury, such as a period of unconsciousness, headache, or vomiting, it is best to postpone any immediate operative measures even though the classical symptoms of shock are absent.

Fortunately, the great majority of injuries of the face are not serious from the standpoint of life and death, and are subject to immediate or early surgical treatment. In this respect, our main object is to re-establish the function of the various tissues of the face and jaws and to eliminate or at least to minimize the visible deformity. Here, even at the risk of oversimplification of the problem before us, I shall discuss the methods used: first, injuries of the soft tissues, and, second, injuries of the bony structure of the face.

## INJURIES TO THE SOFT TISSUES OF THE FACE

The ideal time for suturing soft tissue injuries of the face, such as are seen following ordinary automobile accidents, is immediately, or at least within 5 or 6 hours after the accident. At this stage in most cases, active infection has not yet set in. The invasion of micro-organisms from the skin surfaces or the introduction of others by foreign bodies is limited to the surface of the wound and is easily controlled by mechanical cleaning and débridement.



In treating a superficial wound, the principal aim is to make the resulting scar as inconspicuous as possible. Intelligent surgical procedure will be more readily understood if we analyze some of the problems of wound healing.

1. Other factors being equal non-infected wounds will heal in a better scar line than even mildly infected wounds.

2. Crushed and bruised wound edges become easily infected, and therefore have poor healing power.

3. Children and young adults show a greater capacity to resist infection and the tissues heal readily but clinical observation shows that they are more prone to the formation of larger scars than are older people. Therefore, we must not be disappointed if a carefully sutured wound later develops conspicuous scars.

4. Certain areas produce better scar lines than others. For instance, lacerations over the forehead, temporal region, over the nose, and to a lesser degree over the chin and immediate neighborhood of the lips show less visible scar lines than those on the cheeks and side of the face. Wherever there is a moderately hard base and dense tissues, the scars will be less visible.

5. The direction of the lacerated wound will somewhat influence the scar line. Horizontal scars over the eyelids are almost inconspicuous, yet vertical scars will invariably cause retraction of the eyelid. Similarly scars extending parallel to the skin lines are usually the least conspicuous.

6. Long, straight scar lines are generally more conspicuous than broken, zigzag lines.

7. Finally we must remember that what makes the healed wound conspicuous is not so much the presence of the scar as the fact that the scar is likely to disturb the normal contour of the region where it is located. A depressed or elevated scar causes shadows which accentuate its presence. Moreover distortion of the normal outline of the orbit, the eyelids, or the nostrils resulting from indifferent suturing, from infection, or from contracture of the scar line leads to conspicuous deformities.

Therefore since we know that we cannot prevent the existence of a scar line, as that is nature's method of repair, our primary aim should be to re-form the tissues so that the normal contours of the face will be preserved.

*Operative procedure in primary suturing.* In all wounds that are deep, or grossly contaminated by dirt from the street, tetanus antitoxin is immediately given.

The anesthetic of choice for use in the immediate suturing of face wounds, is novocain either

locally infiltrated about the surrounding tissue of the wound, or injected directly into the sensory nerve supplying the region. General anesthesia is used for children and adults of nervous temperament. When the region is thoroughly anesthetized the surgeon is better able to examine the extent of the wound. The first important step in first aid operative procedure is a complete mechanical cleansing of the field of operation with soap and water and then a careful examination of all the pockets of the wounds for foreign bodies. If a thorough cleansing with soap and water has been done, strong antiseptics such as iodine are not only unnecessary but may be injurious to delicate tissues. The next step is the removal of all the blood clots and *debridelement*—which consists of evulsion of all the loose particles of tissue and bruised surfaces of the wound. This procedure will eliminate most of the infected tissue and leave a clean cut surface for suturing. Adequate hemostasis is the next important step and cannot be over emphasized. Buried sutures may be used to eliminate dead space and to get good contact of the deeper tissues. When a series of buried sutures are applied to the wound the skin surfaces should be sutured with many fine stitches without tension. Lately it has been my routine procedure to avoid straight line suturing in wounds over the mobile parts of the face and in vertical cuts of the eyelids and lips. Instead I have used a broken line with a series of small zigzag flaps. The result has been gratifying particularly in vertical scars of the upper and lower eyelids.

*Wounds with loss of tissue.* Sometimes in a lacerated wound there is a complete loss of tissue, and if the loss is limited to the skin, one is justified in attempting an immediate plastic closure by means of a free or pedicle graft. However such cases are usually so infected that it is necessary to postpone repair until a later date.

*Late primary suturing.* Not all face wounds are clean cut wounds ready for suturing. In fact at the time of hospital admittance a good many wounds are already edematous and infected. There is a great temptation to repair the lacerated tissues as soon as possible, yet one must remember that suturing of even mildly infected wounds never gives a good cosmetic result and complications may even be caused from too early closure.

Therefore, it is fortunate in such cases that there is a broad scope for late primary suturing. This consists of (1) thorough mechanical cleansing of the wound (2) applications of frequent hot boric acid fomentations (3) maintenance of free drainage of the wound. Experience has shown that even badly infected and bruised facial wounds

can be made ready for suturing in from 2 to 10 days by this method

*Powder marks and foreign bodies* Small particles of dirt and powder scattered superficially under the skin present a distressing picture. In some cases the skin has been scraped along in the dirt causing loss of the outer layer of skin in a limited area, with very minute particles of dirt producing discoloration of the bruised area. In other cases, particles of powder are peppered over the face leaving scattered discolored dots over the entire area, often seen in emergency wards following fourth of July celebration. These minute foreign bodies, if not removed immediately, become encapsulated, leaving permanent marks. In a day or two after the accident the points of entry are still open, therefore, it is imperative that vigorous treatment be instituted at this time. Treatment should consist of vigorous mechanical cleansing of the entire affected area with soap and water and a stiff brush, and the marks that are deep and not accessible to bristles of the brush should be scooped out with the point of a sharp knife. To do this, it is necessary to subject the patient to a general anesthetic. It may be a time consuming operation, but it is indicated in view of the gross disfigurement resulting from neglect.

*Injuries involving the bony structure of the face* In a short symposium of this type it is obviously impossible to make more than superficial reference to these fractures.

Wounds associated with fractures become a more complicated problem to treat. The patient usually feels the effect of the injuries and has more pain and discomfort, if the external wounds are communicating with a bone injury, which may be contaminated by oral and nasal secretions. Infection takes place more rapidly. However, there is no counterindication to primary suturing in the presence of fractures provided that such a procedure will not block free drainage.

*Treatment of fractures of the facial bones* Early and adequate immobilization is perhaps the first principle in the treatment of these fractures. Manipulation is most successful when the fractured parts are loose, as the patient is immediately made more comfortable and the spread of infection is limited. The emergency ward may not, however, be equipped with adequate facilities when special appliances sometimes have to be constructed. A delay of a few hours may not be important but a delay of many days may render reduction of fracture more difficult or impossible, the resulting malposition of the fragments may distort the function of the visual or lacrimal apparatus or create malocclusion of the teeth.

*Malar fractures* The majority of malar fractures are simple impacted fractures, the bone being pushed down and back with considerable depression over the zygomatic prominence. No functional disability results from such a fracture if it is left untreated unless the zygomatic arch is pushed against the coronoid process of the mandible. However, loss of the normal prominence of the zygoma is quite conspicuous after the swelling and edema of the soft tissues disappear. The most favorable period for the correction of malar fractures is during the first week following the injury. After that period it becomes increasingly difficult to reduce them.

Comminuted fractures of the malar bone are often associated with fractures of the maxilla. At times, in combined fractures of the malar and maxilla it is impossible to correct the displacement of the maxilla until the depressed malar bone is brought to its normal position. The crushing nature of the injury may cause infection of the maxillary sinus, lower the level of the floor of the orbit or cause permanent diplopia. The main problem in such fractures is to take measures against possible infection of the paranasal sinuses by establishing adequate drainage and immobilization of the comminuted parts by the open method. The maxillary sinus must be opened and drained and all loose or disturbed particles of bone removed. The depressed fragments then may be pulled upward and outward by passing a wire through a drill hole in the infra-orbital ridge and connecting it to a firm headgear with elastic bands.

*Fractures of the nasal bones* In discussing fractures of the nasal bones one must include the effect of trauma on the vomer and cartilaginous septum, and lacerations of the nasal mucosa. While the average fracture may not cause any impairment of function, not infrequently the distorted septum and the adhesions of the soft tissues within the nares cause obstruction to the nasal passages. Therefore, in treating nasal fractures I would like to make the following suggestions: (1) Any blow to the nose causing epistaxis requires an x-ray examination, as in simple fractures there is often enough soft tissue reaction to conceal the depression of the nasal bone and confuse the diagnosis. (2) The fracture should be reduced as soon as possible after injury, especially in children as their bones heal very readily, and a postponement of a week may be too late. (3) Fractures involving the cartilaginous part of the septum should be corrected within 24 hours. (4) Lacerations of the nasal mucous membrane should be carefully sutured to their original position and supported with frequent loose packings. (5) Frac-



Fig. 1. Case. Bullet wound with early infection and considerable first and second degree bruising and burning. At this stage operation is not indicated.



Fig. 2. Photograph of same patient, taken 4 days after operation.

tures involving both nasal bones and also comminuted fractures should be supported by adequate splints following surgical manipulation.

*Fractures of the mandible and maxilla.* At present the nature of injuries demands both surgical as well as orthodontic knowledge.

The surgical procedure first of all consists of careful suturing of the lacerated tissue of the buccal mucous membrane. In fractures involving the alveolar process no attempt is made to save broken chips of bone but these are carefully resected out from the alveolar ridge. The broken down teeth and the teeth involved in the fractured area are also removed. In certain types of fractures of the lower jaw in edentulous patients, direct suturing of the bone fragments is resorted to. However this procedure is not carried out through an external approach as described in surgical textbooks, but instead, the bone ends are exposed through the oral cavity which is an easier method and causes less trauma. We are seldom obliged to resort to surgical procedure in fractures of the neck of the condyle when the head of the condyle is driven out of the socket medially. When it is necessary the procedure consists of forcing the condyle back into the socket, but no effort is made to adjust the fractured ends into their normal position.

In general, dental splints for fractures of the maxilla and mandible consist of utilizing the existing teeth as points of retention. If this is not sufficient utilizing the alveolar ridges—the splints resting upon the ridges—external anchorage which is obtained in certain types of maxillary fractures by fitting a headgear over the top of the head open reduction.

The fundamental aim is to bring the existing teeth into their normal alignment, and this holds

true even if there is definite gap between the two fragments of mandibular bone.

#### SUMMARY

In conclusion, I wish to emphasize the importance of early and thorough care of injuries to the face. Immediate, gentle cleansing and suturing of clean lacerations will avoid deforming scars. Late primary suturing of edematous infected wounds must always be considered. Early immobilization of fractures will forestall marked irregularities of contour of the face. In all severe injuries the serious consequences of infection penetrating the various sinuses of the cranium must be borne in mind.

#### CASE REPORTS

**CASE I.** F. H., female, 5 years of age. This patient was accidentally wounded by .38 caliber bullet on September 7, 1940. After first aid treatment she was transferred to my care and I saw her about 8 hours after the accident. Examination showed lacerated wound involving the right and left corners of the mouth and extending through the mucous membrane of the lower lip (Fig. 1). There was considerable bruising and loss of skin at the left corner of the mouth. Most of the upper anterior teeth were destroyed and several of the lower teeth were fractured.

In spite of the fact that effective first aid treatment had been given immediately after the accident, the wound, even 8 hours later, was already infected and the tissues about the lips greatly swollen (Fig. 2). Primary suturing, therefore, as contra-indicated. After the wounds were gently cleaned with peroxide and tincture of green soap, warm boric acid fomentations were applied constantly. Antitetanus serum was also administered.

On September 11, 4 days after the accident, the wounds were sufficiently clean for late primary suturing. Under ether and ether anesthesia debridement of the granulating tissues of the entire wound was carried out. The bleeding vessels were tied and after considerable approximation and transposition the edges of the wound were carefully sutured.



Fig 3, left Case 2 Photographs taken 1 month after primary suturing Immediate but careful surgery has been carried out, and a good cosmetic result should be obtained



Fig 4 Photograph of same patient taken 6 years after accident. A secondary lip and nasal plastic operation was performed in addition to primary suturing after injury

The patient made a good recovery and was discharged from the hospital 9 days after the operation. At this time the scar lines and the moderate distortion of the left corner of the mouth was less than had been expected, and an eventual good cosmetic result could be predicted (Fig 2).

CASE 2 H O, female, 16 years of age. This patient was thrown from a horse November 24, 1934, striking her face against a stone wall and sustaining extensive lacerations of

the face, in addition to an injury of the spine. She was unconscious for some time. Examination a few hours later showed a deep, lacerated wound extending from the middle of the forehead down over the bridge of the nose and over the upper lip to the vermillion border. Fracture lines which involved the nasal bones and extended down to the maxillary process could be seen quite plainly. The laceration extended into the nasal cavity, separating the mucosa from



Fig 5, left Case 3 Inflamed, lacerated, 48 hour old wound. Operation was delayed another 48 hours (Delayed primary suturing)

Fig 6 Same patient 1 month after operation. There is a good cosmetic result, and still further improvement can be predicted

the nasal bones. There was a zigzag laceration in the median part of the upper lip penetrating the oral cavity. The septum was fractured and dislocated to the floor of the nose. Several of the upper anterior teeth were loose or fractured.

The patient was operated on the last afternoon of November 24, 1934, under vertin, ether and novocain anesthesia. The entire face was carefully scrubbed with tincture of green soap and peroxide and the skin painted with mercuric iodine solution. All the clotted blood and secretions were removed from the nasal cavity with suction tube. The nasal passages were located and packed with gauze saturated with adrenalin. The deep, lacerated wound was then freely exposed and all the clotted blood removed. Three pieces of detached nasal bone were removed and also some small particles of cartilage. The edges of the wound were shaved with sharp knife and scissors, thus eliminating all the torn and irregular edges.

The entire wound including the lip as well as the mucous membrane of the nose was then carefully sutured. At first few deep catgut sutures were applied and the skin was brought together with fine silk. The mucous membrane of the nose as well as the mucous membrane of the mouth was sutured with No. 000 catgut. The left upper lateral tooth which was loose was removed. Robber clamp drainage was applied through the buccal opening of the mouth wound on the side of the face and sutured to the mucous membrane. The head of the patient was then lowered on the table and the fractured nasal bones and fractured septum were repositioned into position with Koch forceps. The anterior part of the nasal passages was packed on both sides with boric strips to hold the septum in position. External dressing was applied supported by dental compound mold.

The patient made good recovery and was discharged from the hospital December 3, 1934 (Fig. 3). She was seen at various intervals, and the scars about the lip and nose gradually became softer. However there developed some thickness under the upper lip, which gave the appearance of "double lip" when she smiled. It was decided to operate again to improve the appearance of the lip, and also further to improve the nasal contour.

On June 8, 1935, the patient was operated on under avertin and novocain anesthesia. The double lip was corrected by excising fold of mucous membrane along the inner labial margin. Contour of the nose as improved by fracturing both nasal bones and reshaping the bridge.

When this patient was seen in October, 1940, the scars of the face were hardly visible and the contour of the nose as well as the lip was quite satisfactory (Fig. 4).

The purpose of presenting this case is, first, to emphasize the effectiveness of immediate surgical treatment when the condition of the patient permits such a procedure and, second, to show that seemingly conspicuous scars following primary suturing will, in the course of time, show considerable improvement.

**CASE 3.** G. N., male, 3 years of age. This patient was injured in a coaching accident February 24, 1940, when he ran into a strand of fire. This wire cut his nose and face and in addition fractured the nose. The child was unconscious and was treated for shock at local hospital here but saline compresses were applied to the wounds of his face. Tetanus antitoxin was also given and the patient was transferred to the Massachusetts Eye and Ear Infirmary days after the accident, February 28, 1940 (Fig. 5).

Examination on that date showed large gaping wound which extended across the root of the nose toward the center of the right cheek, while on the left side of the face it involved large area surrounding the inner canthus of the left eye. There was also an external laceration over the left temple, close to the outer canthus of the eye, and comminuted fracture of the nasal bones which were partly exposed. The entire wound was already infected and covered with grayish, granulating tissue; therefore, it was considered inadvisable to perform primary suturing. Constant warm boric acid irrigations were applied, and this procedure helped to clean the wounds.

Four days after admission to the hospital (4 days after the injury) the patient was operated on under general anesthesia. The face was cleansed with soap and peroxide solution. The loose and necrotic tissues were excised by sharp dissection. The skin wound was closed with interrupted catgut sutures. A drowsed area at the side of the nose leading to the ethmoid cells was left open to granulate in; and the fracture of the nasal bones was reduced in the usual manner. Two small drains were placed deep in the wound for 24 hours. The patient made an uneventful recovery and was discharged from the hospital March 4, 1940, 6 days after the operation (Fig. 6).

# THE LATE CARE OF SEVERE INJURIES OF THE FACE AND JAWS

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THE ways in which an injury may be inflicted to the face and jaws are quite diverse, and, therefore, the resultant lesions are of a protean character. Although such injuries in the past were encountered commonly, within recent years they have become more frequent, largely because of automobile accidents. Usually, a woman is the guest passenger when an automobile accident occurs and has not, therefore, the protective support of the steering wheel to prevent a non-supported forward lurch.

Often, severe injuries of the face and jaws are more tragic than the oftstressed fearfulness of approaching death. Especially, when the victim is a woman, the long years of mental agony that severe facial deformity may cause are deserving of our solicitude, and even in men the psychological handicap imposed by facial disfigurement may blight a promising career.

Whenever the circumstances and condition of the patient permit, most injuries of the face and jaws should be subjected to immediate or early reconstructive procedures. It is, however, common knowledge that often these accidents are complicated by severe injury elsewhere. From necessity, therefore, it may be advisable to delay a reparative operation. The tendency for early swelling to develop and an excessive edema to be manifested after injury is liable to cause the inexperienced surgeon to overlook a depressed fracture of the upper facial region. Careful physical and roentgenological examination, however, should prevent this latter all too common mistake. In the upper jaw region, neglected severe healed injuries are especially difficult to treat. As a rule, however, if the surgeon uses judgment in the selection of the methods at his command, his effort will be well justified.

The four general procedures which one has at his command in the treatment of these deformities may be expressed briefly as (1) replacement of displaced soft tissue or bone, (2) substitution of soft tissue or bone, (3) camouflage of the deformity by the addition or the insertion of various substances to build out contour where replacement or substitution is not expedient, and (4) artificial internal or external prosthesis. The general condition of the patient, extent of the lesion after careful physical and, if necessary, roentgenological examination, the availability of the tissue required for reconstruction, age, sex, and status in life are the most prominent factors which will influence the surgeon in the selection of the course which the reconstruction will follow.

Originally, many of the injuries of the face and jaws which present themselves late were of the compound variety. Therefore, in actual practice, the care of the deformity of both the soft and hard tissues must be considered more or less inseparably. But for purposes of discussion, it would seem advisable to speak of injuries of the soft tissues separately from those of the bony structures.

## SOFT TISSUE INJURY

After the original lesion has more or less healed, the individuals demanding reconstruction of the soft tissues of the face or mouth are of two types: (1) those in whom there has been little or no actual loss of tissue, and (2) those who have suffered sufficient loss of tissue to require the addition of some substitute material.

In the former group fall those individuals with wide or depressed scars (Fig. 1) and those in whom the soft tissues were not replaced or held in their proper position which may or may not have been properly sutured at the proper time. Following a facial injury, in some instances when the soft tissues of the face are severely lacerated or contused or both, it is advisable either to allow the wound to heal by

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Fig. 1. a, left, Result in which the through-and-through incision and also partly lacerated wound of the cheek was rather crudely sutured primarily. Note the stiff scar and its some distance from the incision line and too widely spaced. b, Result year later after careful excision, careful approximation of deeper tissues, and accurate approximation of skin edges plus mild dose of radium which was given weeks after excision.

secondary intention or to approximate the tissues very loosely. For such lesions, as a rule after careful excision of the scar mobilization and readjustment of the deeper tissues, followed by proper deep and superficial approximation and resuturing of the wound, satisfactory contour and a hairline scar of the skin may be offered (Fig. 2: a and b).

When suture marks are present following careless primary suture or late withdrawal of the sutures, the surgeon is likely to be more embarrassed because of the suture marks (Fig. 2) which cannot be removed than by the scar of the primary injury which as a rule can largely be obliterated.

Healed "trap-door" flaps because of the original bevelling of the edges of the flap present a special problem (Fig. 3: a and b). Due to the underlying scar with its tendency to

undergo contraction and the thin edge of the derma which tends to shrink, a humped-up pad of skin and subcutaneous tissue surrounded by an unsightly scar tends to form. Usually one may repair this deformity by raising the flap excising the underlying scar and removing the circumferential epithelial and dermal edge so that a right angled skin edge is obtained. The outside circumferential epithelial rim also should be cut to a right angle. Two small V-shaped excisions may be made at either end of the horseshoe-shaped external circumference to limit its length. The skin edges of the two horseshoe-shaped incisions should be carefully approximated and a pressure dressing applied. This should be left *in situ* for 10 days.

To gain a satisfactory reconstruction in that group of individuals in whom the loss of soft tissue has been considerable the surgeon must take into consideration the breadth and depth of the loss and whether or not the full thickness of some structure such as the ala, cheek, or lip has been destroyed (Fig. 4: a, b, c, d). For the repair of large surface defects, generally a skin graft of a suitable size and thickness for the area and region to be covered is preferable to a skin flap (Fig. 5: a and b). When, however a swinging advancement skin flap from the immediate neighborhood as advocated by Esser and Imre is utilisable it will sometimes give the most perfect result obtainable because of the natural texture and color



Fig. 2. Severe cut across face in which stitch marks are more likely to embarrass the surgeon when he attempts secondary repair than the scar in the suture line.



Fig 3 a, left, "Trap door" flap of lip and nose The surgeon was handicapped at the time of the operation by the amount of edema and swelling b, Result several months after rearrangement of tissue as described in text for "trap-door" flap



Fig 4 a, Loss of about two thirds of lower lip An artery flap from the left upper lip and cheek consisting of full thickness of lip and cheek was turned into lower lip defect It is possible this could have been done early b, Result 3 months after operation c, Almost one third of full thickness of nose was removed Lateral nose rebuilt by means of a skin flap from the forehead The flap was lined with a thick skin graft d, Result 6 months after completion of operation

of the skin of the advanced flap For the repair of surface defects such as those causing ectropion of the eyelids (Fig 5, c and d) in which the circular fibers of muscle are near the surface (orbicularis palpebrum and orbicularis

oris), a comparatively thin skin graft is preferable In the past, thin skin grafts have been considered preferable for the correction of ectropion of the lip, but since the development of the calibrated deep intermediate skin



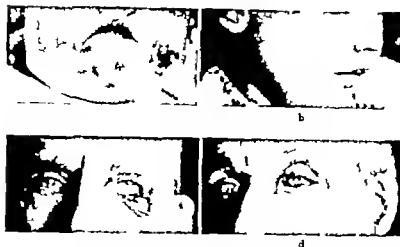


Fig. 5. a, Keloid scar of face. Scar excised and thick skin graft applied. b, Result few years after operation. c, d, Marked ectropion of lower eyelid and scar of left cheek. Correction made by means of thin skin graft applied over scar.

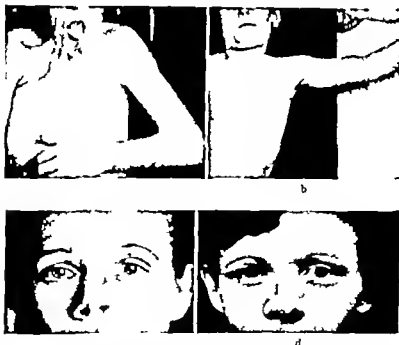


Fig. 6. a, b, Photograph of patient with marked cicatricial contracture of the lower mental region, the neck, the upper chest, the right axilla, and the right elbow. Three operations were necessary to correct this deformity and deep intermediate skin grafts, each of an inch in thickness, were used to correct the contracture. At each operation, good "takes" occurred but there was certain amount of subsequent contracture. The photographs show patient before operative procedures were instituted and 4 months after the last operation. c, Centoural deformity of the nose repaired, and contour re-established by means of skin flap from the forehead. d, Result several months after completion of operation.



Fig 7 a, left This man had lost a good part of the supraorbital ridge and frontal bone. Correction was made by laying back skin flaps over the area and inserting a cartilage transplant of the proper shape to bring out the contour. b, Result 2 weeks later, before the eyebrow grew.



Fig 8 a, left. Lateral deviation of nose due to lateral blow. Result after chiselling the nasal bone from the maxillary processes. Two weeks after operation, a head cast was applied into which a doubled wire was inserted in such a manner as to press on a felt pad over the lateral side of the nose to hold it in position (see Fig 9). b, Result several months later.

graft cut in the last quarter thickness of the skin, practically all facial surface defects of any size, save those of the eyelids, have been resurfaced with this new graft with results very much superior to those previously obtained (Fig 6, a and b).

When there is a moderate contour defect, a skin flap usually will give a result preferable to a skin graft (Fig 6, c and d). The conten-

tion of Maliniak that if one takes a flap cross-wise of the forehead and pulls the neighboring skin together by successive steps without using a skin graft to cover the forehead defect practically no scar is left on the forehead, is a point of value when considering the site from which one is to obtain the skin flap.

For the reconstruction of organs, for building a part requiring two soft, pliable, epithelial



Fig. 9. a, Head cast with doubled treibant so as to lie alongside the nose. A felt pad is inserted beneath the treibant—an efficient and economical appliance which may be applied just before union starts and then is left on about days.

surfaces and some thickness and as a direct covering for cartilage and bone a skin flap has no competition.

As Pickenill pointed out more than two decades ago it is necessary that there should be adequate buccal and labial sulci so that both jaws, lips, tongue, and cheeks can perform their natural and proper functions of both mastication and speech. It is also necessary that adequate sulci should be formed in order that artificial dentures may be worn. For intra-oral contractures in the sulci particular

ly the method of applying an outlay stent skin graft as devised by Waldron and Pickenill has distinct advantages.

#### FRACTURE DEFORMITIES OF THE BONE

To correct late severe injuries of the bony framework of the face and jaws successfully one must understand the essential nature of the original lesion. Probably if the matter is discussed in a regional fashion more clarity will be offered.

**Forehead.** When a healed symptomless depression of the frontal bone, a bony loss of the supra-orbital ridge (Fig. 7 a and b) or an actual loss of substance of the frontal bone is present as a rule the easiest and best correction is given when the superimposed skin flaps are turned back and a properly bevelled and fitted autogenous cartilaginous inlay graft is stepped in the edges of the defect and held by some type of fixing suture. One should not attempt such a reconstruction until at least 6 months have elapsed after any evidence of infection. For a circular loss of substance of the frontal bone McIndoe has been most satisfied with a bone plate taken from the inner aspect of the iliac bone. He points out that the natural configuration of this plate is that of the forehead.

**Nasal bones.** Two distinct types of late nasal bone fractures are seen, the uncorrected



Fig. 10. This girl sustained a crushing fracture of her nasal-buccal, ethmoidal, and bilateral anterior maxillary-bones. a, Shows anterior view of result before corrective measures are taken. A right angled autogenous

cartilage, as inserted over a dorsal piece of cartilage to elevate its bridge, raise the tip, and narrow the base of the nose. b, Front view after completion of operation. c, Lateral view after operation.



Fig 11 a, left Crushing compound fracture of the nose Repaired by inserting 2 superimposed pieces of cartilage at two different operations The second one was a right angled cartilage b, Result after operation

lateral fracture due to a lateral blow and the old telescoping fracture due to crushing frontal blow

Unless the insertion of cartilage or bone will be necessary for correction, fracture deformities of the nasal bones should be attacked as soon as possible Within 3 weeks, manipulation is often successful As time passes, the tendency is for the septal cartilaginous and

bony partition, as well as the bony structures of the arch, to become fixed in a distorted position The septal cartilage may liquefy Secondary changes tend to occur in the alæ and lateral cartilages which may prevent correction even when the mobilization and disimpaction of the bones have been thorough Thus, the problem of correction is complicated after firm consolidation has occurred by the



Fig 12 a, Roentgenogram showing malar lowered bone which is pushed backward and rotated b, Head cast with projecting wire to which a wire passed through malar bone is attached. A indicates the wire c, Roentgenogram

showing a fine steel wire has been passed through the malar bone to hold it in elevated position after disimpaction (A, fine steel wire) (B, heavy projecting wire in the head cast)



Fig. 13. a, left. This man had a compound fracture of the anterior maxilla and his malar bone. The malar bone was displaced backward and laid against the ramus of the jaw and the coronoid process of the mandible. He could not open his mouth. The displaced bone was removed. (4 connectives.) The anterior cheek was fixed. His flap from the neck. The external cheek was repaired by means of a skin flap from the forehead. A prosthesis was used to hold the cheek forward. b, A final operation to raise the orbit has been done after this photograph was taken but has been unable to get the patient to return as yet for a final photograph.

fact that bony manipulation alone is most unlikely to result in a straight nose with an adequate airway unless the septum is corrected either as a preliminary operation or at

the time of mobilization and disimpaction of the nasal bones. Healed lateral displacements and curvatures of the nasal arch and septum should be treated by freeing the nasal bones



Fig. 14. a, Depressed contour deformity of soft tissues and malar and anterior maxillary bones. The lesion was camouflaged by inserting a fatty large properly shaped

cartilage graft subcutaneously anterior to the malar and maxillary bones and artificial eye. b, Final result several months later, lateral view. c, Front view afterward.

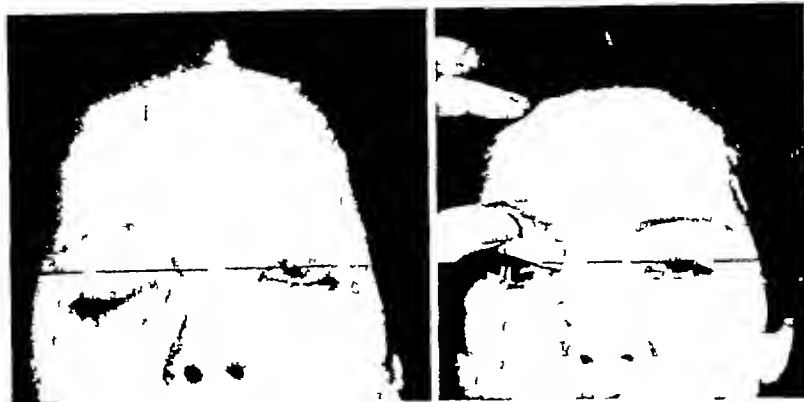


Fig 15 a, left Fracture of anterior maxilla resulting in lowering of the eye globe. The eyelid cannot be opened because of a conjunctival symblepharon. A cartilage graft was inserted subperiosteally above the lowered supraorbital plate to elevate the eyeball and to round out the face anteriorly. b, Final result several months later. A plastic operation was done on the conjunctiva to alleviate the symblepharon. The symblepharon was not entirely alleviated. Since this photograph was taken a skin graft has been inserted into the upper sulcus of the conjunctival sac to free the sulcus contracture which limited the movement of the upper eyelid.

from the maxillary processes with either the chisel or a saw (Fig 8, a and b). In the more severe types comminution of the nasal bones should be radical. Whenever necessary, the nasal septum should be treated by judicious cartilaginous section or submucous resection. In certain instances it is advisable to free the septum at the nasal spine. When one side of the nasal arch is too long, a wedge of bone should be removed from the base of the longer side. As a rule, when the disimpaction and mobilization is thorough, there is so slight a tendency for the nose to return to its former position that it can be kept in position by means of one of the many simple external nasal splints commonly used after rhinoplastic operations. When one of these splints is insufficient, sometimes a through-and-through fine steel wire may be utilized to hook over a dental roll or rubber tube on the side to which the deviation tends and over a cuspid or bicuspid tooth on the opposite side. At other times, it may be wiser to apply definite lateral immobilization by means of a head cast from which projects a double heavy wire which lies along the lateral side of the nose. Beneath the wire is placed a felt pad (Fig 9).

Generally, it will be found to be a useless gesture if one attempts to reduce a late telescoping fracture of the nasal bones. If the base

is too markedly broadened and splayed, it may be wise to narrow the base previously to rebuilding the bridge by sectioning the nasal arch at the maxillary attachments after sectioning the nasal arch in the midline. The septal deformity also should be alleviated at this time. The real mandate in addition to provision for a free airway for the correction of healed crushing fractures of the nose is elevation of the bridge or bridge and tip by the insertion of an appropriate autogenous transplant of cartilage or bone and cartilage. When the tip is depressed, and the alar base broad, a right angled piece of cartilage, the lower end of which impinges on the anterior maxilla in the region of the spine after it has been rongeuired away, is indicated (Fig 10, a, b, c). Not uncommonly, the insertion of two thicknesses of cartilage are necessary to gain a bridge of the proper elevation (Fig 11). Whether or not both of the cartilages are inserted at one sitting will depend upon the degree of mobilization of the soft tissue possible to obtain.

If a septal operation is required, it may be done either at least 2 months previous to the cartilage transplant or postponed until after the cartilage transplant has had sufficient time to be thoroughly acclimated to its new bed.



Fig. 6. This man had sustained compound crushing fracture of his anterior maxilla. The eye globe was not lowered much but the lower eyelid was pulled slightly downward. The defect was principally a contour one. Skin flaps were turned backward. A properly fitted piece of autogenous cartilage was inserted. a, Front view before operation. b, Lateral view before operation. c, Front view after operation. d, Lateral view after operation.

**Malar zygomatic compound.** The malar bone is characterized by a central thick heavy bone standing on four weaker bony supports—frontal, orbital, maxillary, and zygomatic. Blows from different angles produce considerable variation in fracture lines. Most often, the bone is displaced inward downward and backward, and is likely to be somewhat rotated. As a general rule there is comminution of the maxilla which often results in destruction or depression of the infra-orbital plate which if uncorrected results in downward dis-

placement of the globe of the eye with diplopia. The first decision the surgeon is called upon to make is whether treatment is to begin with an effort at disimpaction and elevation of the malar maxillary displacement or whether treatment by camouflage is advisable by superimposing some filling material such as derma, temporal muscle (Gillies) or cartilage above the bone beneath the skin and subcutaneous tissues. Usually if displacement is severe some camouflage treatment will eventually be necessary even if fair reposition is obtained.



Fig 17 a, Wire passed around the mental region of the mandible because of a bilateral fracture of the body. Jaw edentulous. Wire passes through palate, over maxillary nasal surface, and beneath the lip. b, Head cast with heavy projecting wire to which is attached a fine steel wire passed through the mental region of the mandible. This woman had a bilateral malunion with open bite of long duration. Simple interdental wiring of the teeth was insufficient to maintain occlusion. c, Pulley traction after old bilateral malunion of the body of the mandible to stretch the geniohyoid muscles. This is sometimes necessary.



After union has become firm, replacement by means of leverage without dividing the points of union is as a rule unsuccessful. Successful efforts at replacement will largely depend upon accurate diagnosis of the position

of the fracture lines, and the type of fixation used to hold the bone in position after disimpaction and repositioning.

For disimpaction, a double approach is as a rule necessary: (1) from beneath the upper lip across the anterior maxillary wall and (2) through an incision in the upper temporal



Fig 18 a, left External parallel loss of bone causing a contour deformity. Corrected by the insertion of an autogenous cartilage graft. b, Result several months later.





Fig. 9. a, Patient in whom about 4 inches of the mandible was lost because of gunshot wound. b, Roentgenogram showing the bony defect. The ramus of the jaw had been pulled upward and forward. A wire has been placed through the ramus to pull it backward. c, Roentgenogram about a year after piece of the seventh rib had been transplanted into the bony defect. d, Patient's appearance after the bone graft had become solid and firm. Prior to the placing of the bone graft, a good soft tissue bed for the bone graft. This photograph shows external lining which was laid in from flap from the neck. The internal lining was made from flap turned up from the neck.

region so that a chisel may be passed posteriorly to the temporal muscle to a point behind the malar bone. These approaches also allow one to pry the bone forward.

In several cases, the bone has been repositioned and held in position by means of a fine steel wire which is passed through the bone

and attached to a projecting heavy wire laid in a plaster head cast (Fig. 12 a, b, c).

In one individual in whom the malar bone was pushed very markedly medially and posteriorly in such a fashion that it impinged upon the coronoid process and ramus preventing the man from opening his mouth, the bone

was removed as reposition seemed hopeless (Fig 13, a and b) An intra-oral prosthesis was used to support the soft tissues of the anterior cheek after appropriate reparative surgery had been completed

In the majority of individuals with a depressed malar fracture, the most conservative and most successful result is given when the lesion is camouflaged The insertion of a cartilage transplant of the proper size and shape gives a fairly satisfactory result as a general rule (Fig 14, a, b, c) For a minor depression, the insertion of a dermal graft may be sufficient to give correction When the infra-orbital plate is lowered, the insertion of a cartilage graft subperiosteally just above the lowered floor of the orbit may successfully raise the globe, but an entire correction of the diplopia is unusual (Fig 15, a and b) Attempts to correct the enophthalmus by means of inserting cartilage posterior to the eyeball after making a Killian approach have been attempted, but without any noteworthy success

*Anterior maxilla and nasal ethmoidal lacrimal maxillary fracture deformities* As a rule, fractures of the alveolus and supra-structure of the maxilla, unless they are of the pulverizing, crushing type, do not call for late reconstruction In the type of fracture which follows a severe head-on crash with the force falling at the level of the eye globes or slightly below, in addition to a nasal fracture, there results a telescoping of the ethmoidal and anterior maxillary wall compound as has been mentioned previously, when severe malar bone dislocation occurs There is the same tendency for the infra-orbital plate to be displaced with a subsidence of the eye globe (Fig 15, a and b) in anterior maxillary and nasal ethmoidal lacrimal maxillary crushing fractures In addition, in nasal ethmoidal lacrimal maxillary fractures, the inner part of the orbital rim is crushed laterally in the orbit so that the eye globe tends to be pushed outward

Healed depressions of the anterior maxillary wall when rather pronounced (Fig 16, a, b, c, d) may be corrected by filling the depression with cartilage and, similarly, if the infra-orbital plate is lowered, the globe of the eye may be elevated by the subperiosteal insertion

of cartilage above the lowered plate (Fig 15, a and b)

The well known "dish-face" deformity caused by a healed nasal ethmoidal maxillary fracture displacement is difficult to correct Satisfactory elevation of the impaction is hardly possible, but there are several procedures of the camouflage nature which may give quite remarkable improvement both in appearance and function (Fig 10, a, b, c) McIndoe states that sometimes, before 6 weeks have passed, this impaction may be advanced as much as  $\frac{1}{2}$  inch by means of pulley traction Often, the tear ducts become blocked By removal of the intervening bony partition and appropriate plastic operation, the tear sac may be drained into the nose When the splayed inner margin of the orbit is encroaching upon the orbit at its medial rim, the frontal process of the maxilla and the lacrimar ridge should be rongeured away

*Fracture deformities of the mandible* Fracture deformities of the mandible may be divided roughly into two types those due to malunion, and those due to loss of bone

Malunion of the body of the mandible is best corrected by maintaining the fragments in position after sawing across the line of fracture with a Gigli saw There is more of a tendency for non-union to occur after this procedure than there is following the original fracture

Occasionally, one sees a bilateral fracture of the mandible which has united in open bite position The body in this case will need to be severed bilaterally One may experience difficulty in holding the anterior fragment in its proper position by simply wiring the anterior teeth together Three procedures in such a situation may overcome the difficulty (1) a circumferential wire may be passed in the midline about the body of the mandible through a palate drill hole thence over the bony floor of the nostril and beneath the upper lip (Fig 17, 1), (2) a head cast with a long heavy springy projecting wire may be attached to a small steel wire passed through a drill hole in the lower mental projection of the fragment in the midline (Fig 17, b), and (3) in old and marked malunion, the muscles may have to be stretched by pulley traction (Fig 17, c)



Fig. 30. a, Flap over the clavicle has been outlined. The clavicle has been split longitudinally so that one half of the clavicle lies in the flap. The flap has been tubed. The lower end of it has been sutured back in place as a delayed flap. b, About 3 weeks later the flap (including the bony segment of the clavicle) is thrown up into the defect in the chin and the distal end of the flap is used to throw anterior to the tongue to re-form the inferior lining of the lower lip. c, After about 3 weeks the pedicle of the flap is cut and sutured back into place. The pedicle of the tubed flap is held back onto the neck and the granulating area is covered with Thiersch graft.

Occasionally an old fracture dislocation of the condyle is encountered in which the chin has fallen to one side and backward or if

bilateral, the chin may be retrusive and open bite is present. This condition may be corrected by cross section of the mandible so that



Fig. 31. a, left. Gunshot wound of the lower jaw in which section of the mandible was completely destroyed. This case was repaired by pedicled flap in which was embedded bone graft from the clavicle. b, Result 1 week after operation.

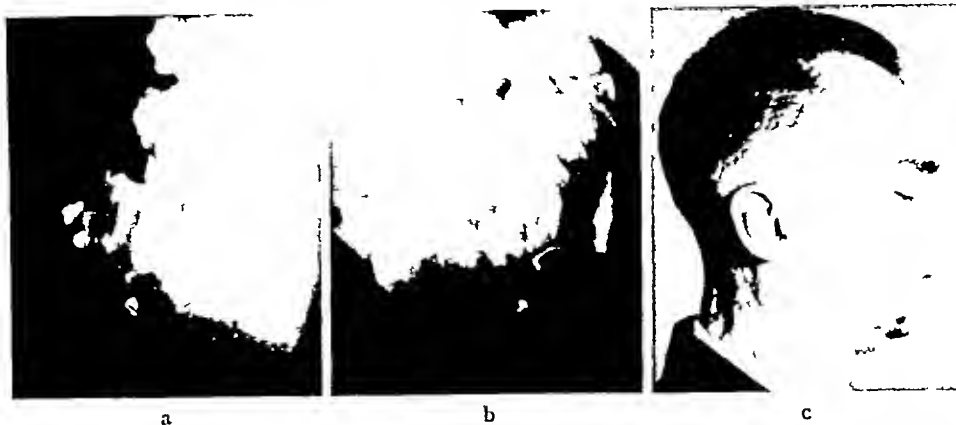


Fig 22 a, Gunshot wound of the mental region which blew away the mental part of the mandible but a fair amount of the tissues of the lower lip and chin remained. In this case a sliding bone graft from the longer side of the mandible was used to throw a piece of bone across the mental region. The lower edge of the mandible was used and the skin of the cheek was left attached to it. Dotted line shows the line of section of the mandible in the long side of the jaw. b Lower edge of the mandible thrown across to the short side and wired in place. The patient obtained good union of the mandible. Later a cartilage graft along the lower edge of the jaw from which the sliding bone graft was cut was used to fill in the contour defect. c, Final result. Defect on short side filled in. The lower lip is a little tight. Front view was nearly normal.

the sectioned bone will interlock when the chin is drawn forward and the open bite corrected by approximation of the anterior teeth (Fig 17, c).

Open bite occurs if a complete supra-structural fracture of the maxilla is allowed to unite in a position lower than normal. Bilateral section of the body of the mandible anterior to the first impinging molar will allow one to obtain anterior occlusion of the teeth.

Parallel loss of mandibular bone along the lower border causes a contour defect which may be corrected by the implantation of cartilage (Fig 18, a and b). As a rule, intra-oral loss is compensated for by prosthesis.

Loss of continuity of the mandible is always associated with considerable dysfunction because the muscles of mastication tend to lose their normal co-ordinated activity. The scar tissue adds to the dysfunction.

When the loss of continuity is not greater than a few centimeters, the method of Delagenière or Kazanjian of placing multiple small pieces of bone and periosteum across the defect may be quite applicable. During the last war, of 38 patients operated upon by this method in the United States Army, 27, or 71 per cent, were successful.

Defects in the lower jaw region complicated by a fairly large loss in bony continuity may be repaired in 4 different ways: (1) by free bone graft, (2) by bone transplanted in a pedicled flap from a distance, (3) by sliding a section of bone from a neighboring fragment without freeing it from its soft tissue attachments, and (4) by the substitution of prosthesis for the loss of about one-half of the mandible.

A free bone graft is most applicable when the surrounding soft tissues are sufficient or easily transferred and when the defect is a long one of the body or the body and a part of the ramus of the mandible. The graft may be taken from a rib or the crest of the ilium. The crest of the ilium is preferable when the angle is absent (Fig 19, a, b, c, d).

Sometimes, time can be saved when it is necessary to add soft tissue lining and covering as well as structural support if all three (lining, covering, and structural support) are transplanted together. A fairly accessible area to obtain the bone and necessary soft tissue is the clavicular area. A split half of a longitudinal section of the clavicle is buried in a skin flap doubled upon itself (Fig 20, a, b and 21, a and b).



# THE IMMEDIATE AND LATE TREATMENT OF INJURIES ABOUT THE ORBIT

## Presentation with Case Reports

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**I**N the treatment of traumatism to and about the orbit, it is necessary to consider not only the early or immediate treatment but also the late treatment. In many instances, late deformities and disfigurements are due to improper and inadequate treatment early in the condition. One might even say that the immediate posttraumatic treatment modifies to a tremendous extent the later condition which can develop. This is true not only in the consideration of defects of the soft tissues but of bone injuries as well.

First, in the immediate treatment of gunshot wounds of the orbit, especially in those patients who will certainly recover, early enucleation, if the eyeball seems to be lost beyond repair, is necessary. A careful débridement should be done with the removal of foreign bodies. It is not at all uncommon that the fluoroscope is required, and at most times it is an aid in this procedure. At times, large fragments and large foreign bodies are so situated that it might be unwise to remove them. When that occurs, the patient should be kept under careful observation, and the surgeon be prepared at all times to reoperate, if necessary. Bone fragments which are completely detached had best be removed. Those still adherent to the periosteum, and by this to the uninjured portion of the orbit, may be spared. Completely detached fragments, however, will not heal in position properly, usually they form a sequestrum and later demand removal. Figure 1 is such an encapsulated sequestrum. Antitetanic serum is necessary, and usually drainage. Figure 2 is the roentgenogram of a large foreign body, so called "punkin ball," which entered the lateral side of the orbit, traversed it, and lodged in the medial wall of the orbit. The eye had to be enucleated, but the foreign body has been permitted to remain in place now for almost 5 years, without any symptoms whatsoever.

The matter of intra-ocular foreign bodies has been omitted deliberately from this presentation.

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This is a subject complete within itself. Many cases of orbital injuries have accompanying neurological conditions, as would be expected. The graver such complications, the less likely it is that the patient will recover. To repeat, débridement, enucleation, the removal of detached fragments and of foreign bodies, and the administration of antitetanic serum are the important factors connected with these conditions. Penetrating or stab wounds without orbital wall complications should be treated with a pressure bandage and with antitetanic serum also.

*Fractures of the orbit.* Fractures of the roof of the orbit are rather likely neurosurgical problems and are seldom, if ever, simple. The same applies to fractures of the inner wall of the orbit. These usually have not only neurosurgical, but also rhinological conditions complicating them. Fractures of the outer wall of the orbit, when simple, are usually reducible by pressure with a stout periosteal elevator applied against the bone from the conjunctival surface at the outer canthal angle. When they are impacted, an incision may be made here and reduction can be achieved in this manner. Usually, however, such injuries must be reduced otherwise. An incision is to be made above the zygoma and through the temporal fossa. A stout periosteal elevator is introduced through that down across the temporal fossa to rest against the fractured portion of the rim of the orbit. Pressure applied there and augmented, as is necessary, by external manipulations, should reduce almost any fracture with adequate alignment. It is quite possible that a fracture here would be so extensive that one must incise, reduce the fracture through the open incision, and then suture the fragments in position, the edges of the torn periosteum being utilized for the introduction of stout catgut sutures. It is seldom if ever necessary to use silver wire sutures. Figures 3 and 4 are roentgenograms of a fractured outer angle of the orbit which was reduced without incision by pressure applied against the fragment through the conjunctival surface of the external canthal angle.



Fig. 1. Roentgenogram of encapsulated sequestrum of rim of orbit.



Fig. 2. Roentgenogram of large foreign body firmly adherent to medial wall of orbit.

Fractures of the floor of the orbit are perhaps the most neglected of all in so far as this primary treatment is concerned. A stout periosteal elevator can be passed into the semilunar fossa, through an incision if necessary from the mouth and with pressure applied against the rim of the orbit marked improvement was obtained thereby even to complete alignment. In some instances, it is perfectly proper to open the maxillary sinus and to reduce the fracture through that sinus only. When this is used, the floor of the orbit can be splinted temporarily by fitting a molded portion of dental stent within the maxillary sinus to support it. The late effects of an unreduced fracture of the floor of the orbit are so serious that every effort should be made to correct them at the time of the accident, if it is at all possible.

Fractures of the orbit which have healed in deformity should not be rebroken. Exostoses and displaced but solidified fragments overriding and causing either a deformity or an impairment of ocular motility should be removed through a clean surgical incision. A depressed eyeball from an old fracture of the floor of the orbit—probably the most common deformity—should be corrected by a costal cartilage graft. A piece sufficiently

thick to raise the eyeball to the proper level is removed, the periosteum on the rim of the orbit is incised and elevated, and this cartilage graft of proper shape and thickness slipped beneath the periosteum. If the periosteum itself cannot then be closed by sutures, an adherent cicatrix will occur which after complete healing must be resected, to obviate a permanent crescentic adherent depressed scar in the soft tissue there. Figures 5 to 8 are illustrations of a cartilage graft correction of a posttraumatic depressed floor and damaged rim of the orbit, the correction being finally completed with a pedicle flap.

Many of these patients will need additional muscle surgery. This is not an especially difficult matter however compared with the surgery necessary for elevating the depressed eyeball. Figures 9 and 10 are the illustrations of a simple depressed orbital floor corrected with a scale of cartilage. The horizontal lines show at a glance the amount of elevation obtained. In Figure 10, the lower lid on the right shows the minimum scarring possible.

In regard to injuries of the globe it is necessary to consider the globe itself and its extra-ocular muscles separately.



Figs 3 and 4 Roentgenograms of case before and after reduction of orbital fractures

A small proportion of cases present themselves with injuries which are without doubt hopeless from a reparative standpoint. Such instances as a massive laceration of the sclera with loss of the vitreous, and the prolapse of the uvea, if they

appear early, should have an immediate enucleation. If, however, there has been an interval of more than 2 days after the injury, ablation of the cornea and an evisceration of the scleral shell is the better procedure. Meningeal infection has



Fig 5

Fig 6

Fig 7

Fig 8

Fig 5 Loss of rim of orbit and the major portion of the floor of the orbit

Fig 6 Immediately after the cartilage graft

Fig 7 Pedicle flap in place

Fig 8 Pedicle of flap returned correction has been completed





Figures 9 and 10. Illustrations before and after similar surgical correction.



Fig. 11. Markedly traumatized eye demanding enucleation.

occurred, though infrequently following the enucleation of an infected contused eyeball. Figure 11 is a markedly traumatized eye fit only for enucleation. Figures 12 and 13 illustrate the primary suturing ring terraced and with tarsal plate and conjunctival suture lines offset from the skin suture lines minimizing these by later notching of the lid margins.

A word here as to sympathetic ophthalmia is especially relevant. This complication can occur in the absence of an open wound. It was seen rather recently in a case of equatorial subconjunctival rupture of the globe from a direct blow. The opposite extreme is also seen. Massive limbal lacerations, when handled adequately, frequently recover even though the injury has been in the so called danger zone. It is rather likely that a chronic irritative condition of the ciliary body or other portions of the uveal tract, following trauma, is absolutely necessary for the development of sympathetic ophthalmia regardless of whether the condition is caused by tissue sensitivity or by bacterial etiology.

In a case of limbal laceration without iris or ciliary body incarceration if this can be closed

surgically the likelihood of sympathetic ophthalmia is not imminent. Prolapse of any portion of the uvea must be corrected. In these, the surgical judgment as to whether or not to enucleate is perhaps the most important factor in the treatment. No one wishes to be responsible for the development of sympathetic ophthalmia. At the same time, the opportunity to save an eye with usable vision if utilized with success, is a far greater achievement than the most beautifully performed enucleation. Prophylaxis in every sense is the most serious consideration in regard to the development of this condition.

The relevant factors in deciding for or against an enucleation can be reviewed. They are given in the order of severity; hence, naturally, are also a chart of ascending imperative indications. (1) The size and the shape of the laceration i.e., the major portion of the laceration being anterior to the ora, posterior to the ora, at the ora, or from the ora extending anteriorly into the cornea. (2) prolapse of the uvea, and the severity of this. (3) the degree of intra-ocular hemorrhage present. (4) the amount of vitreous lost. (5) spontaneous extrusion of lens. (6) collapse of the globe and (7) an immediately sightless eye—this is seldom, if ever to be retained. Further modifying factors are as follows: an iris prolapse must be resected in closure if a scleral wound the ciliary body cannot be pinched therein. Scleral wounds should be sutured. It is not sufficient to cover them with a conjunctival flap and hope that this will adequately bridge the defect. Black paraffinized sutures of 6-0 silk can be passed through the conjunctiva superficially then through the two scleral lips of the wound, and out again through the conjunctiva so that these can be removed readily following healing. After sufficient of these have been introduced and tied, the conjunctival



Figures 12 and 13. Illustrations of the primary suturing terraced to prevent notching of the lid margins.



Fig. 14. a. Partial ptosis from incomplete sectioning of levator. b. Ptosis corrected by a reattachment of the levator. c. Same case to show the normal degree of lid closure possible after the correction.

wound may be closed itself, so that this suture line is well offset from the scleral suture line. It may even be necessary and perhaps wise to use a sliding conjunctival flap. Any wound which passes into the cornea must be closed with such a flap. It is necessary to seal off the anterior chamber early and thus prevent synechiae, not only at the angle but also anterior and posterior synechiae. The late correction of a descemetocoele is a difficult procedure compared to its prevention by the use of such a flap. This applies especially to punctate acid burns of the cornea. As said before, any degree of iris prolapse must be corrected by a surgical iridectomy. All acid burns of the conjunctiva and the cornea, if severe, usually damage the eye to such an extent that vision is seriously endangered. The symblepharon which develops means later correction with mucous membrane. The use of neutral ammonium tar-

trate will minimize this damage more than any other form of treatment. In several instances when, following debridement, mucous membrane grafts were used very early in the course of the treatment, the end-results seemed to be unusually good.

Scleral wounds which pass toward the equator beyond the ora should be rimmed along both lips of the wound with diathermy pin punctures, in the hope that thereby a later retinal separation may be prevented.

The surgery of cyclodialysis, the uneventful correction of limbal ectasia, even the surgery of retinal separation, illustrate the resistance to surgical trauma which the uveal tract possesses. On the other hand, the indiscreet application of the cautery for a small posterior extraction of prolapse has been sufficient to precipitate sympathetic ophthalmia. It seems that the threshold



Fig. 15. a. Partial ptosis from incomplete sectioning of levator. b. Ptosis corrected by a reattachment of the levator. c. Same case to show the normal degree of lid closure possible after the correction.



Fig. 6 Mechanical ptosis from an adherent cicatrix.

between proper and nonpermissible surgical procedures to the uvea is not very wide when chronic irritation is an additional factor.

The therapy of anterior dislocation of the lens into the anterior chamber is upon a sound basis and needs no mention here. The differential diagnosis between this and bloodstaining of the cornea should never be in doubt. Subconjunctival dislocation of the lens through a limbic scleral laceration is a rather serious condition. Posterior dislocation of the lens from contusion and compression injuries is also a surgical problem, but it is not as outstanding an emergency situation as is that of an anterior dislocation.

Another point relevant here, though more important from a prognostic standpoint, is the remarkable number of contusion and compression injuries with massive vitreous hemorrhages. It has seemed that repeated anterior chamber paracentesis combined with subconjunctival injections of a mildly hypertonic salt solution increases, to a great degree, the rate of absorption of these vitreous hemorrhages. In posterior scleral injuries which involve the optic nerve with a resulting secondary optic nerve atrophy, one should be doubly certain that there is no deep orbital

bone involvement. In one such case the diagnosis of such a complication was not made until autopsy following death from a suppurative meningitis. The presence of this complication may mean a radical change in the immediate post-traumatic treatment of the patient. Ophthalmologically it has the same relationship to prognosis as a posttraumatic rhinorrhea has to rhinology.

In regard to traumatism of the ocular muscles, the immediate primary treatment is negligible as compared, in importance, to the later treatment. It is very certain that one would not operate upon a ptosis until complete healing had occurred after an injury. The same applies to the other ocular muscles. Contusion with nerve paralysis, seen rather commonly (as in football injuries) and due, rather probably, to retrobulbar hemorrhage certainly should have nothing except the most conservative treatment. Probable lacerations of the ocular muscles from a perforating wound, as from a shot runner or the end of an iron picket, should have as the immediate treatment only drainage from the depths of the orbit with rubber tissue, and perhaps compression with hot 10 per cent magnesium sulphate solution. Injuries to the lids themselves in such instances should be sutured primarily but not the extra-ocular muscles (Fig. 11). If the nerve supply to these is destroyed then the surgery would be of no avail, and if still intact, later surgery may not be necessary. At all events, one can proceed later with deliberately planned constructive surgery. The correction of the diplopia will then be achieved according to well established principles.

Ptosis may be due to the partial sectioning of the levator with its nerve supply still intact. These instances will oftentimes show after the primary healing a bit of normal lid elevation usually at the inner angle. In such instances, the



Fig. 7 left Posttraumatic strabismic ptosis.  
Fig. 8, center Following muscle and Tenon's capsule surgery.  
Fig. 9, right After levator advancement.

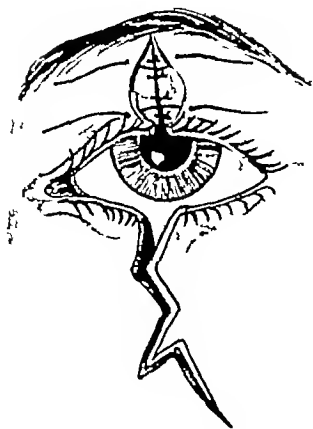


Fig 20 Wiener's suggestion for lid closure as seen in upper lid

surgery is relatively simple. The dissection should release the retracted levator for adequate reattachment to the tarsal plate. Figure 14 shows such a case, the incomplete sectioning of the levator was corrected by this type of reattachment. a is the original defect, b the correction, c the closure possible following correction. In the case of a completely destroyed levator, the ptosis surgery planned should be based upon the utilization of the occipitofrontalis, as in Figure 15. Ptosis from superficial and deep lid cicatrices (Fig 16) to be discussed under the injuries of the lids is a matter wholly of scar resection and resuture.

The later surgery of posttraumatic ocular motor injuries is a bit more difficult, or perhaps more complicated, than the other ocular motor paralyses, nontraumatic in etiology. The former patients will often have Tenon's capsule incarcerated into scleral cicatrices. Mild to severe degrees of strabismus fixus are seen. The elevators are not at all uncommonly paralyzed, are adherent with and to the lids by the scar, and naturally with high degrees of hypertropia. An intact superior oblique muscle can oftentimes be utilized to replace a completely paralyzed internal rectus. Tendon transplants from normal superior and inferior recti are of greatest assistance in the surgical correction of a traumatic external rectus paralysis. They are indicated, however, only when the eye cannot be externally rotated to the midline of the palpebral fissure. Divergent strabismus fixus, especially when accompanied by some exophthalmos and ptosis, can occasionally be rather well held in a primary position by a



Fig 21, left Notching of upper and lower lid before correction

Fig 22 After correction

brutal tenotomy of the external rectus and incision of Tenon's capsule, carried up and down to the edges of the superior and inferior recti and combined with muscle and capsule advancement of the internal rectus. The operation is completed by the application of the suggestion of Reese, occasionally necessary following an orbitotomy (Fig 17), in which buried nonabsorbable sutures are passed from the septum orbitale through Tenon's capsule to the edge of the perosteum at the lower rim of the orbit and back similarly, and there tied. In such instances, a Hess, a Hunt-Tansley, or a fascial sling operation should be considered for the correction of the ptosis. Figure 17 shows a case of posttraumatic strabismus fixus, corrected, as in Figure 18, with muscle and Tenon's capsule surgery, and Figure

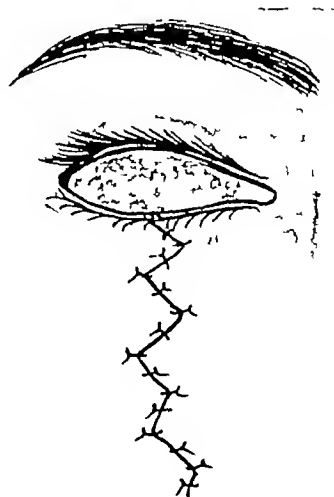


Fig 23 Sketch to illustrate the suture line used



Fig. 24, left. Front view of marked lid defect.

Fig. 5, center. Side view of marked lid defect.

Fig. 7, right. End result.

19 after a levator advancement. Cases of high degree posttraumatic ocular motor palsies may be so severe, when accompanied as they so often are, by extensive choroidal and retinal lacerations and blindness, that, for purely cosmetic reasons, they are best treated by an enucleation with an implant into Tenon's capsule. Later in treating the elevator paralysis, one should not forget the benefit which can be obtained from tenotomizing the contralateral inferior oblique. Also, it is rather likely that an advancement of a paretic muscle should always be combined with the recession of the same sided antagonist.

In treating or handling traumatizations of the lids, the primary surgery is of outstanding importance; this applies especially to such injuries as lacerations at the outer canthal angle, through-and-through tears of the lids, and windshield cuts at

the internal canthal angle running up into the upper and/or down into the lower lid. In soft tissue accidents wherein one is certain that soft tissue has been lost, as a result of the accident, the primary suturing may utilize very moderate amount of the principles of sliding flaps. In these cases, though, it is certain that secondary and later surgery will be necessary. Free skin grafts and pedicle flaps should not be used in the primary surgery of any injury of the lid except under most extraordinary circumstances.

There is quite a bit of difference in handling the primary suturing of lid injuries which lie parallel to the lid margin, and those which are vertical or perpendicular to the lid margin. In both instances, they should be closed in layers. In the first instance the conjunctiva is to be closed with buried 6-0 catgut, the levator in the upper lid and



Fig. 30. Sketches to show the scheme used to release the adhesions and break up the pull of the scars.



Fig 28



Fig 29



Fig 30

Figs 28, 29, and 30 Sketch for closure of inner angle windshield cut and re-establishment of canaliculus drainage



Fig 31



Fig 32



Fig 34



Fig 35



Fig 36

Figs 31 and 32 Lower lid inner angle defect resulting from razor fight.

Figs 34 and 35 Front and side view immediately after

operation to illustrate the exact carrying out of the suggested plan

Fig 36 At the time of the removal of the sutures Some postoperative edema still present.

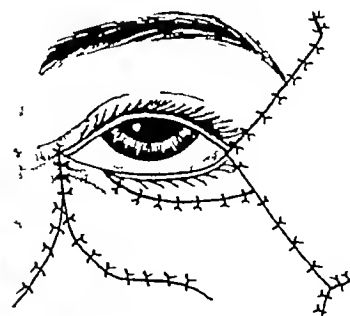
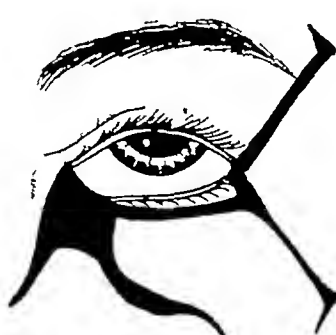


Fig 33 Sketches of scar tissue resection planned before operation

the orbicularis in both lids with 6-0 plain catgut, and the skin closed in accurate approximation with interrupted twisted black silk sutures. These last sutures need to be tied only lightly, approximation of the tissues is the important thing, not strangulation. Incisions and lacerations which

are perpendicular to the lid margin may have their layers of sutures offset one from the other. The suture lines with injuries lying horizontal adjust themselves thus automatically and anatomically. The conjunctival and tarsal plates are to be sutured with burned 6-0 catgut sutures



Fig. 37. left. Ectropion prior to correction. Notice the dense contraction cicatrix.

Fig. 38. Free skin graft correction of ectropion by the use of skin from the hairless skin behind the ear.

The orbicularis is then closed over this, if it is not too badly lacerated. The skin incision is to be offset toward the side with less intact skin surface by resecting 2 or 3 millimeters of the skin along that lip of the lacerations and closing with interrupted sutures.

Notching at the lid margin in such lacerations can be prevented in several ways. Wiener's suggestion is to cut the lips of these wounds crescentically (see Fig. 30), the concavities facing each other. This tends to elongate the suture line and thereby prevents notching. Two tiny tongues of lid margin tissue can be cut at the end of each lip of a laceration and then slivers of tissue from the sides of the incision are cut so that when a final marginal through-and-through suture is placed, these two tongues will mound up or pop out into redundancy. Excess there, following complete



Fig. 39. left. Marked cicatricial thickening of lids. right. After completion.

Fig. 40. After completion.

healing, can be wiped off readily with an application of the actual cautery. However, the most careful approximation of all layers, especially at the lid margin, the less likely will any notching occur. If a vertical laceration can be closed in steps or terraces or inclined away from the perpendicular by tiny triangle resections, it will be of great assistance. Figures 31 and 32 show such an instance. Figure 33 is the drawing to demonstrate the closure. Figures 34 and 35 are front and side views of a marked lid defect with gross contraction cicatrices. Figure 36 shows the scheme used to release the tissues and to break up the pull of the scars. Figure 37 is the end result.

External canthal angle lacerations, when the obliquity at the outer angle is downward should be overcorrected at the time of the primary suturing. Suture the fibers and the raphe of the orbicularis and reattaching the external canthal ligament to the periosteum will achieve this. Those which oblique upward, ordinarily do not need this overcorrection. In closing lid and conjunctival lacerations, one must be careful not to bury the caruncle otherwise an entropion may occur at the inner angle with constant epiphora.

When a lower canaliculus has been cut, a No. 1 probe should be threaded through the lower punctum, to emerge from the cut distal lip of the canaliculus. With the probe then as a handle the cut lid can be placed at its exact anatomical position. The probe should then pass readily into the lacrimal sac. Sutures are to be placed on the anterior and posterior surfaces of the lid, and on the lid margin bridging the laceration, for accurate approximation even to the use, if necessary, of buried 6-0 plain catgut. The major portions of the external end of the probe may be cut off with wire cutters, the end bent away from the lid margin and this probe permitted to remain in



Fig. 41. Wheeler technique correction of upper and lower lids.



Fig 42 The ideal utilization for a pedicle flap

place for about 6 days. Later, some canaliculus probing will be necessary to prevent or correct a stricture. Figures 28, 29, and 30 show the technique and closure.

The later handling of lid traumatism is to correct the deformities from contracting cicatrices or those defects due to the loss of soft tissue. Naturally, these latter will be more extensive and more difficult of repair. The first essential in any of these instances is to study the cases very carefully with photographs and from line sketches. In this way, the surgeon can decide the position of the necessary incisions and the scar resections and the positions and direction of subsequent sutures. He can estimate the amount of tissue which is lost, and how this is to be replaced. Figures 31 and 32 show the lower lid inner angle defects as a result of a razor fight. The sketches of Figures 33, a, b, and c, illustrate the scar tissue resection necessary to correct the defect as it was planned before operation. Figures 34 and 35 are front and side views of the patient made immediately after operation and illustrate the exactness with which the plan sug-

gested could be carried out. Figure 36 is the same case at the time of the removal of the sutures. There is still some postoperative edema present as would be expected. The method of replacing the tissue depends upon the amount lost, the position of the defect, and the amount of scar tissue contamination in the surrounding tissues. There are several other less flexible requirements, for instance, a lost eyebrow should be replaced either by a temporal scalp flap or an occipital scalp free skin graft, and lid margins for cilia reconstruction should be replaced with a free full thickness graft from below the eyebrow.

Full thickness grafts of any type can be obtained from the upper lid on the opposite side, if this is still normal, or from that hairless portion of skin immediately behind the ear. Razor-cut grafts are readily obtained from the inside of the thigh, or, if Paget's dermatome is used, from the skin of the abdomen. The free skin graft cicatricial correction of ectropion, a condition in which lost epithelium must be replaced, is very satisfactorily corrected by any one of a number of procedures utilizing a free skin graft. Figures 37





Fig. 43.



Fig. 44.



Fig. 45.



Fig. 46.



Fig. 47.

Fig. 43. Loss of both upper and lower lid and of the eyeball.

Fig. 44. Correcting pedicle flap.

Fig. 45. The flap raised and attached to remains of lower lid.

Fig. 46. The flap attached to remains of upper lid.

Fig. 47. Pedicle resected, flap incised for palpebral fissure, patient wearing ocular prosthesis.

and 38 illustrate the correction of an ectropion by the use of a free skin graft from the hairless skin behind the ear. Figure 39 is a case of marked cicatricial thickening of all four lids with ectropion, with the loss of the major portion of the right eyebrow. Figure 40 shows the end-result following the use of Wheeler's technique. The intermarginal adhesions were sectioned, some time before, after they had been in place for 4 months. The case was completed with the scalp eyebrow graft as illustrated. Figure 41 shows a similar correction, more severe in degree, with the inter-

marginal adhesions still present, on the left, and in b, the end-result 6 months later.

Pedicle flaps (Fig. 42) If they are to be cut and used, should be lifted and sutured with their long axis always parallel to the lines of the normal muscle pull of the underlying muscles. If this is disregarded, secondary scars may develop, which are quite unnecessary. If massive defects need cervical flaps Snyder's principle of delayed transfer of flaps is used. Massive deformities, involving both the conjunctival as well as the skin surface of the lid, must be corrected with mucous membrane upon the posterior surface if the eyeball is still intact and worth saving. One may not, under any circumstances, permit epithelium to come into actual surface contact with the cornea, nor to lie juxtaposed. If the eyeball has been lost and enucleated, then both the anterior and the posterior surfaces of the reconstructed lids may be covered with epithelium. Figure 43 shows a patient with such a condition. Figure 44 shows the correcting pedicle flap after it had been lined by an epithelial pocket, lifted, and resutured in position to enhance its nutritive supply. Figure 45 shows the flap lifted and attached to the remains of the lower lid. In Figure 46 it is attached to the remains of the upper lid. In Figure 47 after resection of the pedicle and a horizontal incision for the palpebral fissure, the patient is wearing an ocular prosthesis. This reconstruction of orbit and lids can be done by first lining the orbit with a graft as for a contracted socket, thereafter by using the pedicle flap for the external surface of the lid. Pedicle flaps with either a mucous membrane or a skin posterior surface are formed by first making a pocket lined with epithelium or with mucous membrane to the position from which the correcting head of the flap is to be lifted. It may be wise, in all these



Fig. 48. T-bar flaps for socket reconstruction.

# SPAETH IMMEDIATE AND LATE TREATMENT OF INJURIES ABOUT ORBIT

cases, to lift the flap and then to resuture it in its original position once or twice, wholly or in part, before it is finally transferred to its correcting position. This enhances tremendously its nutritive blood supply, hence, its viability.

When conjunctival defects accompany a lid defect and the flap is not the correcting procedure to be used, a free mucous membrane graft for the conjunctival defect should be the first procedure. Symblepharon with partial lid damage as an accompanying ectropion is the usual example of such a situation. Intermarginal adhesions are a necessary step in the free skin correction of ectropion, and these should not be released until all scar tissue contraction has ceased.

Defects for correction in which there is no deficiency of soft tissue must depend for success upon a complete removal of all cicatrix. The necessary undermining cannot be done unless it is adequate. This is seen in such instances as cicatricial ptosis and contraction lagophthalmos. When a free skin graft is to be used, adequate scar resection is an important factor. The inability to achieve this is perhaps the outstanding indication for the use of a pedicle flap. During the dissection for releasing a cicatricial defect, one must release with great care such structures as the orbicularis fibers, the canthal ligaments, the lid margins, and especially the deeper muscles responsible for the normal lid folds—the levator palpebrae in the upper lids and the lower crescentic fibers of the orbicularis. Following the normal lines of tissue cleavage simplifies a dissection decidedly. Pedicle flaps are indicated in situations where it is impossible to release or remove all scar, hence, this matter of scar resection is least applicable to that procedure.

The repair of a contracted socket, the result of a traumatic enucleation, always is accompanied by dense scars and the loss of considerable conjunctiva.

In these, one must remove boldly all cicatrices in the orbit. The dissection should form an inferior cul-de-sac level with the lower rim of the bony orbit—incising the periosteum there (not to have an inferior cul-de-sac of this size later, but to form a sheet of scar tissue adherent to the periosteum which will assist in maintaining a satisfactory inferior conjunctival fornix). The dissection into the superior fornix must pass up and backward, but sparing the levator palpebrae,

otherwise, ptosis will result. Figure 48, a, b, illustrates two such situations. In a and lower cul-de-sac alone was lost, in c and entire socket was replaced by a dense obliteration of scar.

When the graft is cut, to cover the mold as fit as to the size of the dissected socket the surface of the mold must be certain that the entire surface of the mold is covered. Excess graft adjusts itself by necrosis and lysis, but an inadequate graft means fresh scars and adhesions, granulation and an unsuccessful result from the surgery.

Cicatricial enophthalmos as the result of retrobulbar posttraumatic suppurative cellulitis is a not uncommon and most distressing situation. Little if any surgery can be done to restore the lost ocular motility. The fixation which is present is a combination of true ocular motor nerve paralysis, actual destruction of the ocular muscles and muscle—Tenon's capsule—eyeball cicatrice. If usable vision is still present, it is worth while attempting to correct the enophthalmos. The position of the eyeball can be improved by transconjunctival internal and external canthal angle incisions, the resection of the scar, certainly its wide release, and the introduction of rolled bolsters of tensor fascia femoris retrobulbarly. Some of these can be placed between the muscles and the eyeball, and others, especially above and below, between the muscle and the roof and/or the floor of the orbit.

The postoperative dressings for plastic cases are important. Free skin grafts must be applied with a fair amount of pressure with a dressing which will not creep. A splint of dental stent molded to the defect just before the graft is placed seems to be most satisfactory. The pressure dressing of a pedicle flap should not be as firm as for a free skin graft, and it must not compress the nutrient pedicle. Free mucous membrane grafts into the conjunctiva can be held in accurate approximation for several days after operation by means of a silver conformer, perforated in the center, so that the conformer is not in contact with the cornea. Absolute hemostasis is necessary before any graft can be placed in position or any dressing applied.

In the late treatment of these soft tissue defects, one must not lose sight of the important rôle which adequate massage can play in minimizing scars and releasing those already present.

# HISTORY AND PRESENT STATUS OF OPERATIONS ON THE LABYRINTHINE CAPSULE FOR OTOSCLEROSIS

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THE results in hearing obtained by fenestration of the horizontal semicircular canal present problems which are still mostly unsolved. This surgery has opened new vistas of inquiry and research. It has demonstrated the paucity of our knowledge of the physiology of hearing. It brings into serious question concepts on diagnosis and classification of hearing defects hitherto held as established.

We are wont to consider surgery in the light of the relief or cure it affords for pathological lesions. In the type of surgery I am discussing the restoration of a physiological function toward normalcy is the goal sought. The concept that by a surgical procedure the microphonetics of the structures of the ear shall become re-established to function normally and cause a deafened patient to hear presupposes a comprehension of these. In this premise lies most of the handicaps in this field, under which the otological surgeon works.

Surveying the exploratory surgical efforts to achieve successfully restored hearing acuity I find that obstruction and confusion have been brought about by the record of many observations and postulates which from a scientific standpoint, are unacceptable.

There is difficulty in summarizing end-results from this operation. The operations are recorded. The obvious successes and failures can be tabulated. The operations done by one man can be added to those done by another and a grand total of successes and obvious failures can be summarized but still that leaves us no nearer a solution of the problem, because there has been no standard criterion for the selection of cases for operation. Different types of cases are included among the successes as well as among the failures after surgery.

In other words, it is almost impossible to establish a standard for the comparison of similars. Inherently the cases differ although the deafness is seemingly similar. The same audiometric findings are possible in deafness of varying causation. It must be assumed that each

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surgeon has set for himself a criterion to indicate that operation would be successful. Then why in the same hands, and with the same technique do failures occur? I have done exactly the same thing on successive patients and in each instance have employed the same criteria in selecting the case for operation, yet failure resulted in some while in others there were astonishing successes. I assume that the difficulty has its origin in the fact that this surgical procedure is aimed at restoration of function and not at removal of the pathological process.

Notwithstanding these considerations, the literature reveals attempts to sum up the totals of results from different surgeons. Of course deductions thus made are open to scientific skepticism. In fact, this scientific skepticism has a place in evaluating case reports from any individual source which reports too large a sum total of material, all classified as otosclerosis and reported as having been operated on, successfully or unsuccessfully as the case may be. In such reports, I see an endeavor evident to make a diagnosis based on pathological condition in the deafened patient, and to mark up success or failure on his functional activity. The lessons which the surgical procedure might teach regarding functional rehabilitation are minimized or lost. It is an assumption that the technical steps of this procedure are based on proved concepts. It is likewise assumed therefore that if the surgical steps in the technical procedures are properly carried out, the expected favorable end-results on functional restoration will be accomplished. The reason for this paper is to help clear up the misconception as to the present status of surgery for otosclerosis.

The exact clinical diagnosis of otosclerosis is almost impossible in fact in most of our otological institutions the number of cases definitely diagnosed as otosclerosis is small. I myself still use the Lucase triad of raised lower tone limit, prolonged bone conduction and a distinct hereditary factor as criteria for the classification of cases. Among those patients with chronic progressive deafness I find many who cannot be said to be deaf because of otosclerosis, according to the Lucase triad. Hence it is safe to assume that even

in a given surgeon's practice patients of inherently different categories have been subjected to a specific operation, and the successes and failures recorded as the result of the procedure rather than as a result which would naturally follow in a specific type of case. Holmgren may be expected from this criticism.

Too much stress, particularly in America, seems to be laid on a definite technical procedure and its minutiae. There is further confusion because fundamental factors concerning the surgery of otosclerosis are being complicated by an effort to popularize an endaural approach to the goal of operative endeavor—the fenestration of the horizontal semicircular canal and the covering of such fenestration by a tissue the external surface of which shall be in contact with sound waves and which shall aid in re-establishing better microphonetics in the deafened ear.

Whenever bone tissue or soft tissue is traumatized, whether accidentally or surgically, healing ensues. After surgical fenestration and covering, the goal sought is the achievement of healing without regeneration of bone which would close the fenestration.

Success or failure needs consideration from various aspects. First as to healing, the wound made must heal promptly, with a dry ear, an intact drum, and an epidermized wound cavity. Second, as to function, success or failure cannot be judged wholly by the ability of the fenestration to remain patent; patency is estimated by producing a positive reaction to the fistula test when the site of the fenestration is touched with a cotton-tipped applicator. At re-operation, I have observed definitely open bone fenestration although the findings on fistula tests were negative by touch. In one such patient, even touching the exposed membranous labyrinth with a cotton-tipped applicator failed to elicit either nystagmus or vertigo. This patient, when subjected to the Barany labyrinthine tests, showed normal function of all semicircular canals. Let me emphasize here that the lack of a positive fistula response on touching the site of fenestration should not always be assumed to imply that the fenestration has closed. In many cases it has closed, but in others the surgical procedure was successful. Other factors have produced the negative reaction to the fistula test, among which may be mentioned local labyrinthine adhesions walling off the site of the fenestration from the rest of the membranous labyrinth.

Furthermore, the postoperative positive reaction to the fistula test when the site of the fenestration is touched is not a sure indication that the

functional re-establishment of hearing acuity has been attained. In patients operated upon by others as well as in some of my own, although at repeated examinations I have invariably obtained positive fistula test reactions, the hearing acuity has remained unimproved since operation. Therefore when a positive reaction to the fistula test is used as the sole criterion in estimating the case as a success the observation is unsound. The surgical technique may have been successful in keeping the fenestration open, but the result as to restoration of hearing should nevertheless be considered a failure. From these observations the conclusion is inevitable that the maintenance of a patent bony fistula is *not the sole factor* necessary to improve hearing acuity, or, conversely, that all patients do not show functional hearing improvement when a fenestration is made and maintained in the horizontal semicircular canal.

The dramatic demonstration of suddenly acquired increased hearing acuity at the operating table at the moment when the perilymphatic space is entered has little scientific implication, and no deduction should be drawn from it. It is more important that the surgeon visually recognize the penetration into the perilymphatic space than place reliance either on the suddenly exhibited nystagmus or on the increased hearing acuity because, if the membranous labyrinth has been accidentally injured, the dramatic exhibition would nevertheless be present. The absence of all these phenomena because of deep general anesthesia or somnolence from hypodermic medication during local anesthesia, however, does not preclude good after-effects and a satisfactory end-result, as some of my cases demonstrate.

#### HISTORICAL DATA

It manifestly is impossible within the reasonable scope of this paper critically to annotate and document all pertinent publications which in their successive appearances in otological literature since 1779 trace an *evolutionary progression of development* of this type of surgery for the improvement of hearing acuity. I will content myself with a brief account of the principal contributions up to the one stage endaural technique. Recent reports will be touched upon only as they present factual observations bearing on the present status of this type of surgery.

Since 1779 propositions, techniques, and case reports have appeared revealing attempts to improve hearing. These range from efforts to achieve permanent openings in the membrana tympani, to tenotomies of both the tensor tympani and the stapedius muscle, to extraction of

the malleus and the focus and even efforts to extract the stapes.

In 1877 Knebel (18, 19) removed the stapes, and thus opened the osseous labyrinthine channels. A transient improvement in hearing resulted. In 1897 Passow reported that he had constructed a protective drill with which a hole could be made in the bone of the promontory just below the oval window and adjacent to the insertion of the foot plate of the stapes. The immediate results on the hearing acuity were amazing. The tinnitus also disappeared. These improvements were found to be transient, however, and because of the opposition of Pollitzer, Catzoltus, Lieberman, Botey, and Denker—all great authorities in otology—the operation was discarded.

In 1898 Alderton opened the labyrinth at the oval window. Only temporary hearing improvement resulted. Farad in 1899 reported having operated upon 11 cases, after extensive animal experimentation. He made fenestrations in the cochlea by removing small sections of the rim of the oval window. His reports were, on the whole, favorable. In the same year, without knowledge of the work of Passow, after opening the promontory, he placed a Thiersch graft over the fenestra. At first the hearing was good, then equivocal. In 1899 Floderus also, without knowledge of Passow's contribution after extensive cadaver studies, employed for the location of the fenestra, the ampulla of the external horizontal semicircular canal near the bony lamella bounding the vestibular perilymphatic cistern of Retzius. What his functional results were are not quite clear from his report. In 1903 Jenkins (14, 15, 16) reported on 2 cases upon which he made fenestrations in the horizontal semicircular canal. For a covering he used a Thiersch graft in one case and in the other employed a skin flap made from the external auditory canal wall. His improvements in hearing acuity were transient, and the end-results were somewhat better than before operation. In 1904 Barany suggested fistulization of the posterior vertical semicircular canal. He showed that improvement of hearing was procurable but the results lasted only a few days. In 1917 Holmgren, after making a fistula, immediately covered it with an elastic membrane. The fistula was placed at the upper part of the anterior vertical semicircular canal, after the bone between the dura and the fistula was removed and the dura was allowed to act as a covering for the fenestra. The hearing in one patient, thus operated on, was good. The result, however, was only transient. Holmgren suggested another feature, the excision of a piece of the dura and the use of

the arachnoid membrane as covering material. This was, as far as I am able to ascertain, never performed in a living patient. In 1917 Holmgren operated on the promontory of the cochlea and used a mucoperiosteal flap for covering tissue. Reporting in Paris in 1920 Holmgren conceded that his results as to improved hearing were only transient and his end-results were negative. In 1923 he reported that while the improvement in hearing was not permanent, it lasted a longer time. During the course of observation of patients operated upon, he noted a progression to the hearing loss in the ear not operated upon, but that in the ear operated upon the hearing did not go below the level held at the time of operation. In other words, the progressive loss of hearing seemed stopped in the ear operated upon, even though hearing in this ear did not permanently improve.

About 1922 Fremel reported a case in which he had made a fenestration in the posterior semicircular canal. The improvement in hearing was transient, but the hearing loss remained stationary on the side operated upon.

In 1924, Barany made the first report of a two-stage operation. The first stage was an antrotomy and fat was placed in the cavity. The wound was permitted to close and heal. After 4 to 6 weeks, the cavity was re-opened, the horizontal semicircular canal exposed and opened. The previously placed fat tissue was pushed into the fenestra, and the wound reclosed and healing allowed to proceed. But Barany, working with gonges and without magnifying glasses, could hardly avoid little traumas to the membranous labyrinth and small hemorrhages into the lumen in the canal. In Barany's technique, it is to be noted that after opening the canal, he first implanted a piece of fat and thus blocked the opening, then he enclosed the fat and the opening with a piece of rubber dam about the size of a pea, to make it kneadable he warmed this piece of rubber dam and pressed it into the opening of the fistula. The results as to hearing were primarily good. They lasted only 2 weeks, however. He reports his results as follows: Directly after the canal is opened the hearing increases from near the concha, where once is heard before operation, to a distance of several meters. After the canal opening is closed, an appreciable loss of the newly acquired hearing is noted. Nevertheless hearing is still better than before operation, for conversation is comprehended at a distance of several meters.

About 1926 we again find Holmgren attempting a fistulization of the horizontal semicircular canal, which he immediately covers with the

mucoperiosteum of the ampulla. This resulted in a very great improvement in hearing, which lasted for a few weeks. In some cases improvement in hearing was not so marked, but it lasted somewhat longer.

In 1924 Sourdille (27) reported on fenestration of a horizontal semicircular canal. His is a multiple operation. In the first stage he explored the middle ear and attempted to isolate it. He termed this procedure an atticotympanotomy, simple or combined, with an internal plastic with a tympanic hinge. At the second operation he opened the external horizontal semicircular canal and occluded the fenestration by a thin epidermic membrane. Each stage of the procedure was done under local anesthesia and with strong adrenaization. Because of what followed it seems wise to give the details of the pioneer work of Sourdille. He not only merits the distinction of having persisted in the search for a solution of this problem, but he is credited by Holmgren with having restimulated him after "failures" again to study this problem. Sourdille's technique embraces the following: (1) mastoid trepanation, with careful elevation of the soft parts of the external auditory canal from the bony canal wall, (2) mobilization of the tympanic membrane only in the upper half of its circumference, with the cutaneous lining of the external auditory canal, (3) a resection of the "osseous bridge" of the external wall of the attic, and of the tympanic ring, corresponding to the portions of the tympanic membrane which he mobilized. This done, a larger view of the attic, the tympanic cavity, and the ossicles is obtained. This procedure he terms "simple atticotympanotomy." It permits exploration of the fenestra ovalis and the lesions of the ossicle. (4) Removal of the body of the incus with or without resection of the head of the malleus. This step he terms "combined atticotympanotomy." (5) His "internal plastic." With a tympanic hinge the flap obtained from the posterior superior wall of the membranous canal is lowered inward and placed against the internal wall of the attic. By its adherence to the attic wall the tympanic cavity is hermetically closed and separated from the mastoid region. There then ensues an interval during which epidermization takes place in the opened parts of the mastoid cavity.

A few months later the second stage is undertaken when the cicatricial lining of the mastoid cavity is sufficiently thin and transparent. Then trepanation of the prominence of the external semicircular canal is performed. This takes place in the following sequence of steps: (1) The retro-

auricular wall is reopened. A piece which is destined to be replaced over the opened canal wall, is traced and cut out of the cicatricial flap. The tympanic cavity is not to be reopened. (2) The prominence of the external semicircular canal is trepanned by rubbing with special rubbers made for this purpose. (3) The epidermic flap is placed over the new orifice of the fenestration, thus closing it and preventing any infection of the internal ear.

The first stage of Sourdille's procedure is not concerned in improving hearing, but is merely a preparatory measure to provide a means of closing the labyrinthine fenestration. Sourdille, however, does report that he has observed a slight amelioration in deafness, *more marked in the opposite ear* (italics mine). He also observed diminution of the previously present tinnitus in both ears. During the second stage of the multiple surgical procedure, he makes the following observations:

"During the operation no matter how thin the osseous wall of the semicircular canal may be, no improvement whatever of hearing takes place before the perforation of this wall. At the very moment when the operator perforates this wall, the patient complains of dizziness of short duration (from 1 to 2 seconds) after which he hears with incomparable clearness and intensity. This reappearance of hearing as well as the dizziness coincides with loss of a very small quantity of perilymph. This can only be seen under the microscope with a magnifying power of ten diameters. The improvement in hearing depends on many factors."

During one operation, Sourdille observed that hearing at the initial opening into the semicircular canal, which was very small, immediately was improved and the patient comprehended the low spoken voice at a distance of 40 centimeters from the ear. When the semicircular canal opening was enlarged hearing acuity was increased to 2 meters for the same spoken voice. In all his cases the low pitched sound was heard best. This was particularly true in patients in whom before the opening was made the high pitched tones were better heard. Sourdille makes the following additional observations:

"In order to make possible the perception of low speaking voice at a distance of 2 meters, at operation, it is necessary that the labyrinthine trepanation be laid open. If one covers it with an epidermic flap, immediately the voice is not perceived at 1 meter, or at 80 centimeters, or even at less distance. The maximum audition seems to correspond to the penetration of the sound waves through the labyrinthine fistula thus made. If, now, I apply paraffin gauze, covering alternately the tympanum or the epidermic flap, I obtain, according to the former degree of deafness, and the state of the flap, hearing equally well by the tympanum or by the labyrinthine trepanation. This indicates that hearing can be perceived equally by the tympanic route

and the fenestra rotunda, or by the labyrinthine orifice and the scala tympani.

If I cover the tympanum and the orifice of the labyrinthine preparation at the same time, the low voice can even then be heard at a few centimeters and the high pitched voice is understood with an intensity and clearness unquestionably better than before operation. The Schiwaach has the same value as before, and the Rinne remains negative.

Sourdille believes that the end-results depend entirely upon the condition of the flap. If it remains thin, closely applied, the improvement of hearing lasts without change.

Immediately following Sourdille's presentation before the Royal Society of Medicine, Mr. Harold Kisch (30) reported that he had performed some operations in cases of deafness and catarrhs of the middle ear. He had considered the question whether or not to make the new opening through the semicircular canal or through the promontory. He had decided on the latter. He employed a simple method, exposing the middle ear and then using a small trephine worked from a dental engine. He entered the promontory through the outer wall of which he removed. He immediately closed the gap of the promontory using a skin graft taken from the thigh. At a session of the Royal Society of Medicine in 1912 Kisch demonstrated 11 cases. His end-results could not be reported as during the first World War his papers had become lost and the patients scattered.

In 1936 Holmgren (11) reporting to the Third International Oto-Rhino-Laryngological Congress in Berlin, made a report on surgery for otosclerosis. His procedures then were as follows:

Under local anesthesia, an antrotomy is performed with most careful hemostasis. The anterior lateral wall of the sacculus endolymphatic is then uncovered. At this point in the operation, he notes an immediate improvement in hearing. Then, preferably using a chisel, fistulas are made in the horizontal and in the posterior vertical semicircular canals. Sometimes he also puts an opening into the anterior vertical semicircular canal. Each fistula is made fairly long, 4 to 5 millimeters. The endosteum is removed

without injuring the membranous labyrinth, and the fistula is closed as much as possible. As soon as the fistula reaches the canal, the hearing increases promptly and constantly. In fact, all patients hear better and conversation at greater distances than the length of his operating room. They hear at least at distances of 2 meters. He now enlarges the aditus and antrum and soft prosthesis is laid into the antrum and into the fenestrations. Much Holmgren believes prevents collection of blood and wound secretion, and supplies an elastic wall for the fistula. This prosthesis is so placed that it crowds the openings made somewhat, to prevent closure during the healing process. As prosthesis he employs various substances—a thin rubber bladder (filled with air, physiologic salt solution, or fat), pieces of gutta serena, or more recently fat tissues. In addition he also reports that he has coated the antrum with gold leaf and then put the fat prosthesis on top of the gold leaf. He believes that this prevents an undesirable growth of the

fat tissue to the membranous labyrinth. Everything being placed in position, he closes his original incision with Mikkel clips and secures healing by primary union.

Holmgren makes the following observations:

The improvement in hearing at the time of operation is constant and astonishing. During the period of healing hearing is reduced in some cases to the pre-operative state but he found it even more than before operation. In the majority of his cases (he reports on 34 in this communication) greater or lesser improvement in hearing is attained, which in certain cases is even progressive.

In October, 1937 Sourdille (8) came before the section of otology of the New York Academy of Medicine and reported on his latest procedures and summarized his cases. Sourdille now proposes a surgical technique which usually consists of three stages but sometimes requires more than three stages.

The first stage is performed entirely within the external canal. It consists in lifting the cut thick cutaneous soft parts, fibrous bands, and perosteum of the posterior superior semicircumference of two-thirds of the external auditory canal. The operation to accomplish this, however, is carried out through a postauricular incision. It may be done through the external auditory meatus, provided this is sufficiently wide. The interval after this procedure is utilized to obtain surface of membrane from which perosteum has been removed, a supple cicatrix, but resistant and without sebaceous glands. The time which generally elapses to accomplish this he puts at between 6 to 8 weeks. The second stage is carried out entirely in the middle ear. An incision is made through the original postauricular scar. The previously made thin cicatrix is separated from the posterior superior canal wall. The cicatrix is now found to consist of new skin and scar tissue and also of the upper border of the drum. This step Sourdille calls an internal plastic. Next a resection of the mastoid process is undertaken and the aditus and attic completely everted of all cell structure, thus bringing into view the incus and the head of the malleus. The joint between these two parts is opened and the ossicles separated. Then the head of the malleus is carefully resected, caution being observed not to injure or puncture or tear the membrana tympani or to displace the incus which should be maintained in its high lying position and its posterior and its inferior articulations conserved. The previously prepared flap is then elevated and its bleeding surface applied to the incus, its internal surface to the attic and the aditus, and as far as it will reach placed over the floor of the antrum. The middle ear is thus hermetically

sealed in its superior portion. The procedure is ended by covering the lower part of the exenterated mastoid cavity with an external plastic flap made up of scraps of skin and muscle elevated from the inferior surface of the mastoid process.

Now a second interval of time is allowed to elapse of about 6 to 8 weeks, and observations are made of the transformed ear through the external auditory canal. Generally the meatus will be found widened and communicating directly with the mastoid cavity. A large vestibule has been formed behind the curve of the horizontal semicircular canal which is covered by a more or less thin cicatricial pedicle of cutaneous tissue. This is found communicating with the modified tympanic system now found comprising the membrana tympani and the so-called "internal plastic," the surfaces of which are continuous in their superior half circumference.

The *third of labyrinthine stage* consists in lifting up the endomastoidal flap at the level of the external semicircular canal. This canal is then opened, extreme care being exercised not to injure the membranous labyrinth. As soon as this opening is obtained, there is noted an increase in hearing 10 to 20 times better than the pre-operative hearing acuity. The cicatricial endomastoidal flap is now replaced over the fenestration. Sourdille makes the following observations regarding the hearing.

The hearing which ordinarily has been decreased in the days immediately following the operation, when cicatrization is complete, is measurably increased. It is better even than that observed on the operating table. With tuning forks, the return of aerial hearing for low pitched sound (64 and even 32 double vibration forks) are heard. The Weber is changed, lateralization toward the side not operated upon and even the Rinne can be positive on the side operated upon.

Sourdille remarks that "unfortunately the success is ephemeral." In from 4 to 6 weeks he has observed that the aerial hearing diminishes, the Rinne test reaction becomes negative and the results of the Weber test equivocal. He thinks this is due to closure of the labyrinthine fistula, because of the reconstruction of rigid bony deposits which close the fistula.

These bony replacements, Sourdille considers, do not attain the thickness of the primitive bony canal wall. In most instances they do not attain thickness of more than a few tenths of a millimeter. Therefore, he undertakes a supplementary operative procedure to remove this bony film. This he calls "touching up an operation." The

hearing is then re-established and often only then will this gain in hearing be lasting.

Sourdille's tabulation of results comprises 140 patients upon whom he operated about 400 times. The hearing results were very good (hearing improvement was measured by distance in which given sounds could be heard) and showed improvement in increase of distance of 10 times that of the status before operation. These equalled 40 per cent. Those whose hearing distance improved only 5 times that of the status before operation equalled 14 per cent. Recently through improved technique, he obtains good results in 80 per cent of his patients, and of these, 60 per cent show an increase in hearing distance 10 times that of what they had before operation. He had no fatalities in any of his 140 cases.

Following Sourdille's report Lempert described a new one-stage procedure which embodied all the features of Sourdille's operation. He used burrs and claimed to use the Shrapnell membrane as covering for a fistula produced in the horizontal semicircular canal. His operations were performed endaurally. This was the first American contribution.

Other current reports are based on the pioneer work here reported. Otologists in this country and England are at present trying out the Holmgren, Sourdille, and Lempert techniques, but their cases are too recent to be of value in estimating end-results.

#### THE FUNDAMENTAL OBSERVATION

There is now available a very creditable record of surgery to improve hearing. In each and every procedure which is reported, it is recorded, and my personal experience substantiates it also, that as soon as the osseous labyrinthine capsule is opened, there is positive demonstration that the deafened patient hears better than before fenestration was undertaken. And this is observed in varying types of cases which exhibit deafness as a symptom, whether or not that deafness is caused by the lesion known as otosclerosis. This is an important scientific fact. Nor does this fact lose its significance if subsequently this initially improved hearing acuity is lost. This repeatedly observed fact upsets our ideas regarding the pathological lesions which, from audiometric tests followed by histopathological studies have given us a conception of the lesion held responsible for the deafness. In other words, if the lesions rendered the patient deaf, how account for the immediate recovery of the function of hearing upon fenestration in an exactly similar case? Surely it may be surmised, if these studies are



correct, that similar lesions are present in the hypothetical case cited, and we know that the effect of a fenestration operation does not immediately reach ganglion cells in the cochlea. This premise may be stated, thus: patients complaining of deafness and tested by the means at our command—the audiometer forks, voice etc.—are actually deaf only in relation to the media used to test them. Even those greatly deafened, who by the means we employ to test them show what are called islands of total deafness, are not actually deaf for this sound wave frequency because often when the amplitude of vibration of the same sound wave frequency is greatly increased—as for example by use of an organ-pipe—these patients will hear some note. Probably an actual acoustic nerve lesion with its accompanying dysfunction is the only exception to this generalization. In this connection it is of interest to note that Lucæ believed that even when he had positive evidence of stapes ankylosis this finding did not indicate that the patient was actually deaf. So profound a student of otosclerosis as Albert Gray of Glasgow wrote in 1923 that the deafness of otosclerosis throughout a large part of its course is due “rather to suspension of the function of hearing than to its actual destruction.”

The retention of the newly gained improvement in hearing acuity constitutes the very essence of the problem which this method of treatment seeks to solve. *One way to achieve this* is to devise a means to maintain the surgically made fenestra in the labyrinthine wall. Let me at once add that not in all cases in which this surgically made fenestra remains open, does hearing acuity remain at its initially acquired improvement level, but in some instances it gradually drops to its prior level of recorded hearing loss. As a corollary therefore, the second fundamental problem for solution is to find the means to differentiate between the cases prior to surgical intervention. The finding of a permanently maintained open fenestra giving a positive fistula reaction, a healed surgical wound, an intact tympanic membrane and open eustachian tube, totally unaccompanied by maintenance of improved hearing acuity leaves the situation unsatisfactory. The success or failure of enduring results of the procedure still remain unpredictable and the patient even in the most competent hands, must take the gamble on the expected results.

#### EFFORTS AT MAINTENANCE OF AN OPEN FISTULA

Because of the obvious finding that, when fenestration is done and the surgically made window remains open for a time, hearing acuity

also is improved, it is easily comprehended why such intense efforts have been made to keep the fenestra open.

The studies may be divided into groups. The surgical studies of Holmgren (13) are noteworthy. A fistula covered with subcutaneous fat in 1 patient resulted in improved hearing for 3 years. Holmgren also tried covering the fistula with a mucoperiosteal flap and with gold leaf and a tissue lined with connective tissue and covered with pavement epithelium was also employed. He has not yet reported the results obtained from the last set of experiments. Regarding technique he recommends that the perosteal layer of the labyrinthine wall be removed as far as possible. The endochondral layer will not heal and the endosteal layer and endostium should be removed as completely as possible. The semicircular canal should be opened on its concavity or at its side. His experiments with the application of prolonged pressure to produce pressure erosion he suggests plugging the habenular canals in the bone with bone-dust, and also suggests the use of electrolysis through the application of various metals to prevent bone regeneration and encourage bone atrophy. Finally he is now experimenting with irradiation through the application of radium or mesothorium. To date, nothing of positively definite value is available. The experiments are not concluded, and for Holmgren the question still remains unanswered.

Soundille (28) has a very complex technique to maintain patency of the fenestra. In substance it consists in the use of a connective tissue flap covered with pavement epithelium. After repeated revisions which he euphemistically terms “touching up” the site of the fenestration by removing newly formed bone lamellae which close the area, he eventually has some remain open because he says he exhausts the regenerative power of the bone. I record what he states but doubt the scientific value of the reasoning. Lempert (23, 24) established a postulate in his reports in which he stresses that covering the fenestra with Shrapnell's membrane is the necessary factor for success in keeping the fenestra open. Additionally the use of polishing burrs and burnishing burrs and of a 24 karat gold burr to impress gold dust particles into the exposed bony surfaces is advocated. Most anatomists and many otological surgeons have serious doubts as to the possibility of stretching Shrapnell's membrane to reach and cover the fenestra placed in the horizontal canal. Lempert's own failures and reported revisions in themselves lessen the strength of his contention, to say nothing what

soever of Sourdille's report of 74 per cent successes in 140 patients Sourdille never employed any kind of burr in any of his cases, and he makes no pretense of employing Shrapnell's membrane to cover the fenestration His record, on its face value, is every bit as impressive as Lempert's Incidentally, Lempert's first report of having operated on 23 patients of whom 22 had persisting fistulas needs revision when his Boston presentation is studied In this report the failure to maintain an adequate fistula among these 23 patients amounts to 39 per cent It is presumed that he employed not only the burrs but also the so called Shrapnell membrane as coverage Holmgren also suggested employing the dura and the arachnoid over the superior semicircular canal, which he had fenestrated Employing the dura in some instances and the arachnoid in others, he used a tissue which contained no periosteal stroma, nevertheless the fistulas closed, and the hearing acuity reverted to that before operation One is forced to the conclusion that the regenerative power of the bone itself is the factor at fault This factor, which is nature's method of repair, must needs be nullified or guided in some way if success is to be achieved in keeping the fenestra open

As a matter of fact, there are successful cases on record in which fenestration was done by different instruments and by the use of different tissues to cover the fistulas Among those who used other tissue than Shrapnell's membrane is Campbell The Guggenheims report a case which they observed, and they state specifically "that the claim that the *pars flaccida*, or Shrapnell's membrane, is used to cover the fistula is not accurate" Among my own cases, I have never been able to get Shrapnell's membrane to reach far enough to cover the newly created fenestra in either those which I term successes or those which are not I do not think that Lempert's contention in regard to this factor in his technique will stand the test of time and experience

The experimental studies of Canfield and the Guggenheims, while valuable contributions in themselves, leave the main question still unanswered Canfield endeavors to solve the question as to what differences occur in the surgically traumatized bone by the experimental effects of the instruments used in the surgery The influence of heat and friction from the burrs, the injury to bone cells by the burr, and the possible diminution of the bone's regenerative power—these all engaged his study He concluded that the response of vital periosteal bone differs significantly when defects are made with different

instruments, even when the defects were universally covered with the same tissue According to Canfield, the essential point in keeping the fistula open is the management of the bone itself with less regard for the nature of the tissue placed over the defect Canfield credits the bur-nishing burrs with inhibitory power over bone regeneration The Guggenheims, on the other hand, fail to substantiate this contention

Neither the Canfield nor the Guggenheim experiments were carried out upon semicircular canals This raises objection to conclusions drawn from these experiments The Guggenheim report, however, anticipates this criticism by stating "The fact that the labyrinthine capsule consists of both membrane and cartilage bone in no way affects the experiment, as all new bone formation, whether in the labyrinthine capsule or elsewhere, is by membrane-bone process The ontogenetic phenomenon of the transformation of cartilage model into bone model is *strictly* an ontogenic occurrence, and never a repair process In the final analysis of osteogenesis in artificial fistulas, the individual characteristics of primary germinal tissue (mesenchyme) will doubtless prove to be the determining factor just as they are in such conditions as chondrodystrophy and osteogenesis imperfecta and in connection with individual potentialities for fracture healing" Believing osteogenesis can be impeded by vitamins, Kend has undertaken a study of diet with combinations of vitamins to inhibit bone regeneration Although his reports are as yet unavailable he generously furnished me with his data, so that I might try them also

To summarize it can be said that no way to keep the fenestra open has yet been devised which successively applied will successively give similar results Neither the use of burrs nor the application of a particular tissue to cover the fenestra assures positive results in succeeding cases with any degree of certainty This is true whether in reference to the cases of one surgeon, or of different surgeons Conversely, good results are reported by different surgeons who have used different instruments to make the fistula and who have used various types of tissue to cover the fenestra

I am still as much at a loss to account for the successes I have had as I am unable satisfactorily to explain my failures, for I have used similar technical procedures in either instance and have encountered no untoward happening to complicate the issue In other words, I cannot predict the probable outcome in a given case because as yet there are no criteria available upon which to

predicate success, nor have I found anything in the published reports of other workers, which would make prediction of end-results more certain. In passing I may remark, that I have encountered untoward happenings in some of my cases—torn flaps, perforations of the membrane tympani, and secondary infections of the middle ear spaces—all of which if the current literature is to be credited, should have doomed the patient to ultimate deafness yet in some of these patients there was a persisting open fistula with improvement in hearing acuity. Why? I cannot yet find the answer.

#### THE RÔLE OF THE INCUS AND THE EPI TYMPANIC SPACE

The rôle of the incus is still unsettled. An ankylotized stapes articulated with an incus but disconnected from its connection with the head of the malleus when the head of the latter is amputated, as is done in the currently employed techniques as first suggested by Sourdille and now part of the so called Lempert operation, leaves the question of what use does the retention of such an incus possess. One of the best functional results I have thus far obtained from this operation was in a case in which the incus was removed.

I may add that studies on the rôle of the incus are in progress, and when deductions are warranted report will be made. The entire question as to the necessity of surgically disturbing the tympanic and epitympanic structures is under survey. Prompted by the work of Sourdille, a reconstruction of the tympanic cavity a resection of the head of the malleus, and its necessary concomitant—opening into and partially obliterating the epitympanic space—are now the operation of choice. This popularity has resulted from the incorporation of part of Sourdille's work in the technique advocated by Lempert which not only be but all his pupils follow without actually comprehending why. The scientific reasoning upon which these procedures are based is totally unconvincing and the theories are not proved by factual observations. There are reports of temporary improved hearing acuity in cases in which neither the head of the malleus nor the epitympanic space was involved in the technique. Of course, failure eventually resulted in such cases as regards permanently improved hearing. These failures were due to closure of the fenestration and did not depend in any way upon the technical procedures upon the epitympanic space.

As has already been recorded in my preliminary report, in some of my patients fenestration has been done without surgically touching any of

the epitympanic and the tympanic structures. In others I have followed Sourdille's suggestions and have amputated the head of the malleus and obliterated the epitympanic space. A sufficient number of patients has not been operated upon and the time elapsed since operation is too short to permit a comparison of results at this time.

Another observation regarding tympanic structures, the epitympanic space, and the ossicular chain should be mentioned. In a preliminary report a year ago I presented audiograms taken before and after fenestration in a patient upon whom radical mastoidectomy had been performed in 1918. At the time the patient came under observation, the ear had been dry and healed for years. In an endeavor to better his hearing acuity with the patient's consent, I performed a fenestration upon his ear. The ossicles, and the tympanic structures were missing as a result of the well performed radical mastoidectomy. The old wound area was covered with a thin epidermized lining and this was used to cover the fenestration. Healing rapidly ensued, and the ear was dry. The fenestration was open and gave a positive fistula test. Hearing acuity was very definitely improved as shown in the audiometric charts and in the conversational ranges. Figure 1 shows the maximum improvement obtained. Hearing improvement was maintained and the fistula remained open almost 8 months, then gradually the fenestration closed, and hearing acuity dropped to that before operation.

The improvement in hearing acuity transient though it was and dependent upon keeping the fistula open, is a fact of great scientific significance. It is a fact that the early pioneers in this type of surgery obtained temporary improvement in hearing acuity upon performing fenestration. This fact has become the basis of all the elaborate techniques since laboriously built upon this one outstanding scientific observation. Therefore, we must study and evaluate the fact established by my observation, namely, that in a patient with the tympanic cavity missing, with the external wall of the epitympanic space ablated, and with the malleus and the incus absent, the fenestration of the horizontal semicircular canal resulted in improvement in hearing. The later loss in the newly acquired hearing acuity paralleled and coincided with the gradual closure of the surgically made fenestra. Do not these observations make us doubt the accuracy of our present concepts as to the rôle which the tympanic cavity and its ossicles play in the inherent acts concerned with hearing? We must build our knowledge from this observation as a basis. In my opinion the

maintenance of the fenestra is the greatest technical factor in retaining hearing acuity and all additional details upon which so much stress has been put, seem less important in the solution of our problems. I shall not here discuss the newer theory regarding the physiology of hearing which the observation just recorded and other studies under way suggest. In addition to this case I shall cite others each of which is a negation of the ideas which the most propagandized technique is tending to spread and because they demonstrate that comparable results are obtainable by totally different technical procedures.

Another observation is noteworthy. If one examines the bone conduction audiogram, taken under conditions of masking, in Figure 1 with 30 decibels of the same note as tendered to the examined ear, a loss in bone conduction is revealed, reaching its maximal loss at the 2048 frequency cycle. During the period in which hearing was improved and the fenestra remained open, this masked bone conduction was markedly improved, and this was true in more than one examination. If the accepted theory of how bone conduction comes about is to be maintained, then we lack a reasonable explanation for this finding. On the other hand, it is logical to assume that the improved bone conduction after fenestration is a factual observation and that our prior held concepts on bone conduction—how it eventuates and its significance when showing a loss, need review and study as to factors in establishing diagnosis. This observation brings into question the rôle played by the ossicular chain in presenting bone conduction. In addition the diagnostic criteria on the condition of the acoustic nerve which we are habitually wont to deduct from diminished bone conduction is also questioned. In my case, bone conduction was diminished but was improved after fenestration despite the absence of the major ossicles and membrana tympani.

#### THE METHOD OF SURGICAL APPROACH

I need add but a word regarding the endaural approach to the antrum and the epitympanic space. Inherently there are many reasons why I disapprove this approach. These reasons have no bearing upon the fundamental questions with which this paper is concerned. The postauricular route has many obvious advantages over the endaural route. I believe the sound judgment of operating otologists will bear me out in this premise. There is no step in this field of surgery that can not be more easily done with the postauricular than with the endaural route, whether

it applies to the epitympanic space, the head of the malleus, the sulcus tympanicus to free the drum and make a tissue to use as coverage for the fenestra, and the fenestration itself.

#### DANGEROUS EXPERIMENTS

It may not be amiss to sound a note of warning regarding one experimental surgical effort, reported incidentally among a mass of other material. The merit of the procedure was never debated or even commented upon in the report of this work. I refer to the revisions undertaken by Lempert in the cases he lists as Cases 88, 71, 72, 97, 56, 8, and 106 in his Boston presentation. In these cases he employs pavement epithelium to cover the fenestra, turns the epithelial side toward the open bone wound, and attaches the blood supplied raw side to the meatal flap. He thus covers the fenestra with a membrane which does not attach itself to the fenestrated bone. This he contends retards bone regeneration. I am willing to concede that this may be true, but every student of medicine knows that pavement epithelium should never be buried in tissue but should be kept in contact with air, and it should be so placed that the inevitable exfoliation from pavement epithelium can find easy egress externally. To this fundamental conception of pathology I believe most plastic surgeons also subscribe. The reverse side of this implanted flap converts itself into living matrix, and Lempert actually is implanting the beginnings of future pseudocholesteatomatous growth if the graft lives. As we know, such growths develop slowly and these patients may eventually—unless our basic knowledge of pathology is at fault—come to grief because of the buried epithelium. What will happen then, as the result of pressure erosion from accumulated desquamation surgically located in contact with the membranous labyrinth, needs no prophet to foretell.

Another word of warning should be said concerning the Lempert reports. In his original publication, he reported 23 cases and of these only 1 fistula failed to remain open. In his second publication (Boston presentation), however I find that 9 of these same cases are listed as having required revisions, some more than once. Among these, in 4 vestibular function was lost or impaired. Among the additional cases included in the 120 patients upon which the second report is based, are 4 others which likewise suffered serous labyrinthitis. This serious outcome was the result of the operation itself and because of it, Lempert was prompted to state "revision of the fenestra involves a much greater risk to the

membranous labyrinth than does the original fenestration." With this conclusion I am fully in accord, and I have done no revisions after my first experience with one. In that case nothing untoward happened, but the dangers inherent in the procedure were so apparent that I have never attempted again operating upon failures, and I would warn the profession against permitting their patients to undergo such revisions. It is better that the hearing acuity revert to the status before operation than that the patient undertake so great a risk of losing his hearing and thus be unable to procure for himself the hearing improvement that an artificial hearing-aid apparatus could bring him. When this type of surgery was first proposed, Holmgren, Sourdille, and I minimized the risks of damage to the membranous labyrinth which are taken by patients under the precautionary aseptic surgical measures usually employed. All these surgeons prided themselves on an absence of any labyrinthine injuries and reported none having happened. This is particularly true of Sourdille who performed 400 operations, revising fenestrations often more than once. The meticulous care as to surgical minutiae and asepsis of which Lempert writes and speaks seems to leave us at a loss to account for the hazards to which his patients were subjected. No otologist of experience, I dare say will minimize the danger which a serous labyrinthitis entails. Unless this type of surgery which carries with it the danger of labyrinthitis is controlled, we shall sooner or later be confronted with the tragedies subsequent to an established labyrinthine suppuration and meningeal infection. That this is a grave danger is evident when I point out that while Frederick estimated the usual occurrence of labyrinthine infection to be only about 1 in 100 cases of *middle ear suppuration* in Lempert's report there were 8 labyrinthine infections in 150 cases.

#### SELECTION OF CASES

The literature furnishes few details which could be used to create a standard for the selection of cases which would be improved by this operation. Current publications imply that the deafness caused by otosclerosis may be helped. The diagnosis of otosclerosis is almost impossible to make clinically at the present state of our knowledge. Hence an approximation to such a diagnosis is all that can be hoped for. It becomes increasingly important, therefore, that prior to subjecting a given patient to this type of surgery a rather prolonged period of observation of the patient—if necessary over a period of months—is desirable

before the final decision is made. In such a study the impression gained by one consultation and examination is checked and rechecked a clinical estimation of the patient is obtained a comprehension of the mental and psychic make-up of the individual is developed and ancillary examinations regarding endocrine disturbance metabolic dysfunctions, and other pertinent factors become part of the case history. This period of observation often presents changes in the audiometric readings too and ranges of variation prior to operation can be established. Usually every one working in this field agrees that good bone conduction, observed under conditions of masking, is at least a desirable condition but that patients whose audiometric readings show a curve indicative of acoustic nerve dysfunction are not good prospects to submit to operation. Holmgren has suggested a detailed study of the drum and the external auditory canal in addition to the classical data to determine the presence of otosclerosis. This study should include a consideration of the thickness of the skin and its dryness an estimation of the amount of subcutaneous tissue the presence or absence of cerumen the rapidity of inducing, or the absence of cough (tickling) and "ocular reflexes" the movements observable of the membrana tympani—which segment moves most, what adhesion restricting motion can be demonstrated and, finally a minute study of the movements observable in the ossicular chain. These observations are made through the precision Bruning Seigle otoscope. In all my own cases these observations have been made, in addition to the recording of the usual data from otological examinations.

In cases which present most of the factors usually recognized as comprising the classical picture designated clinically as otosclerosis, the external auditory meatus is wider than usual, the skin thin and atrophic in appearance with little subcutaneous tissue apparent, cerumen absent, and the posterior superior segment of the drum moves most readily while the rest of it does not. The drum is thin, almost transparent in spots, and the vascular reflex is sluggish or absent unless prolonged efforts are made to evoke it, when it can be produced. The movements of the ossicular chain are generally impeded, although under negative atmospheric pressure in the external auditory canal the excursion outward of the upper segment (above the short process) of the malleus is possible.

Regarding the postulates of Holmgren and reviewing my own case histories as applied to them, I must not in passing a contradiction in

the fact that Sourdille seeks to submit to the operation patients who present a wide and straight external auditory canal, with a large middle ear which is vascularized and resistant

Roentgenography thus far has not been helpful in adding either diagnostic data or criteria useful in selecting cases for surgery. It has given me in each of my cases aid in studying the gross bone structure to determine the presence or absence of pneumatization and the type of cell structure which is present in the given case. Perhaps when the results of planographic studies of the labyrinthine capsule and the middle ear are completed, reports may become helpful in fixing pre-operative data valuable in selecting cases suitable for operation. Sourdille uses stereographic roentgen examinations in his efforts to select his cases. He prefers the type in which the zygoma wall does not pass beyond a vertical plane through the posterior border of the condyle of the mandible.

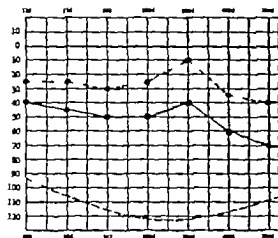
In my own patients, I have had all types of temporal bones to deal with: large pneumatized bone, the infantile type of small celled bone, and also the sclerotic type. In most instances, both in the material upon which I operated and also in that routinely examined by roentgen-ray in the clinic, pneumatized bone has been predominant.

The stricter the standards observed to set data for the diagnosis of otosclerosis, the less material seems available to subject to operation upon such a diagnosis. The healthy skepticism exhibited by Holmgren in his statement concerning Sourdille's report illustrates this point. "I am skeptical when I read of a patient who could (only) hear loud voice near the concha before operation, and at 60 to 150 centimeters after operation, especially when the author considers that hearing has become 60 to 100 (why not just as well 150?) times improved." I, too, am skeptical of the kind of material selected for this type of surgery, when I fail to find that detailed audiometric and fork tests have been recorded numerous times both before and after operation. My skepticism is increased when I read of vast numbers of patients who have had this operation since from a pool comprising my clinical material and my private practice amounting to over a thousand deafened patients I was only able to find about 25 cases during the period from December 1, 1937 to September 1, 1940—the period during which most of the many cases reported in the literature were diagnosed and the operation performed.

#### SURGICAL RESULTS

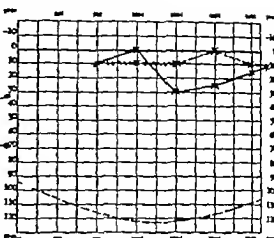
I shall make no attempt to summarize the cases in which patients have been subjected to

operation, nor to tabulate successes and failures. I have already alluded to the difficulties of making such estimates of success in an evaluation of this type of surgery. The cases reported come from differing clinical categories and results are due to the application of different surgical procedures. All the patients have one factor in common—they are deaf. Some may have had otosclerosis. I am sure not all of them did. In all patients, fenestration of the labyrinthine capsule through operation on the horizontal semicircular canal has been done. The case may be regarded as having a successful outcome if the fenestration has remained open. *That is a surgical success.* We also must record whether the functional hearing has been sufficiently improved to be of practical value. *If both are accomplished the case has reacted favorably to surgical therapy.* We should avoid comparing one surgeon's results with those of another, as each of them is performing a different procedure, probably upon patients differently selected. Not even my own cases should be added together to be tabulated as successes or as failures as far as a given surgical procedure is concerned because I am still "sampling" clinical material and submitting different clinical types of cases to different types of surgery in an endeavor to find the minimal surgical endeavor necessary to improve hearing acuity practically. Manifestly, those cases in which I have left the tympanic structures untouched at this time should not be compared with the ones in which these structures have been surgically disturbed. The end-results of two stage operations by the Sourdille technique cannot be computed with those of one stage operations of a different type. These differing techniques should not be compared until at least enough of them have been done to permit an estimate for each group. Until then only are comparisons possible between one group and another. Such basic surgical studies demand time, careful selection of suitable material, and meticulous bedside and postoperative observations. The literary essays, written by men not actually engaged in doing this type of surgery, add little to our knowledge by the sketchy outlines of cases rather than the detailed reports of case histories themselves. These essays consist principally of compilations of large numbers of cases, in all of which the same thing has been done over and over again, and of a tabulation of the successes and failures taken haphazardly without specifically giving in detail the criteria of selection or the most exact diagnosis possible of the cases. In these reports and essays I see little effort to find the factors which are causing the repeated failures



Air conduction.

Fig. Record of the improved hearing acuity in radical mastoidectomy done 20 years ago. Fenestration done on December 8, 1935. The improvement was present



Bone conduction.

both for air and bone conduction (masked). It heard 5 months, then the fistula test became negative, and hearing returned to status quo ante operationem.

Adding up the successes for a given surgical procedure may be practical from the standpoint of private practice but it hardly rates serious consideration on our part as a scientific contribution toward the advancement of our knowledge.

I have followed the reports of all these surgical endeavors since they began to be published. One could wish that some of them had had the benefit of editorial supervision to prevent 2-A audiometric records being placed in comparison with those made on 6-A audiometers! Additionally the stress in our current American literature and, for that matter also in the presentations before our scientific assemblies is to a great extent not concerned with even a beginning of a discussion of the many questions at issue but seems to be designed and specifically arranged in an attempt universally to teach a specific surgical technique whose value has not been successfully established. Lempert, a protagonist in this endeavor, is even now ranging far afield from his own advocated procedures, in seeking answers to the problems which 1 of his patients present whose fistulae are still open but who have had no improvement in hearing. He likewise is seeking the why and wherefore of the bad results in 20 other cases among the 20 he recently reported. These 41 cases (of the 120) had the benefit of his technique and skill. Were Utopian results obtainable by the meticulous adherence to the detailed minutiae of his technique, 120 consecutive successes should have followed the operation in his hands. The actual record, however, tells a different story.

#### PERSONAL CASES UNDER OBSERVATION

To date I have accepted, studied, and operated on 26 patients, performing different operations on them. One patient had both ears operated upon, thus making 27 operations in all. These cases are divided into the following groups:

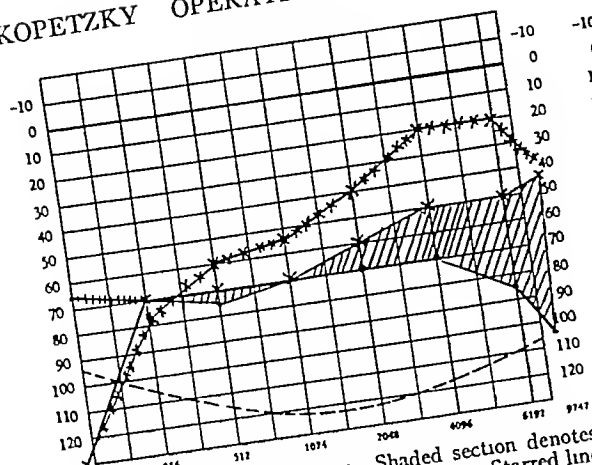
1. Radical mastoidectomy subsequently fenestrated. First stage, Sourdille operation (cases not yet finished).
2. Second stage (completed Sourdille operations).
3. One stage, 1st tympanic cavity and structures untouched.
4. One stage, epi-tympanic space obliterated, head of malleus aspirated and focus removed.
5. One stage, epi-tympanic space obliterated, head of malleus aspirated (focus intact).

Total

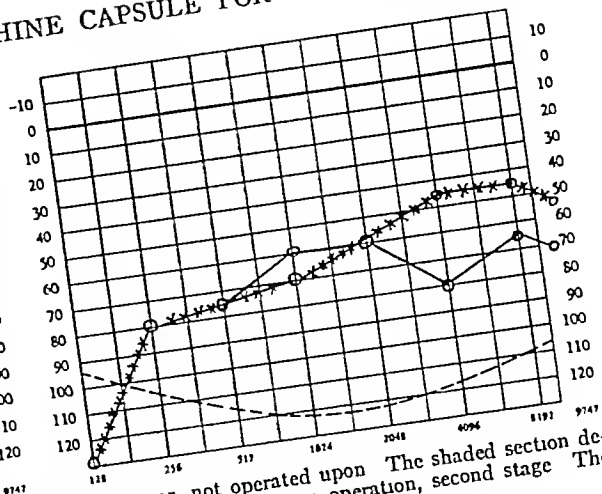
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All operations were performed through the postauricular route, and in all the horizontal semicircular canal was fenestrated. It is important to record here for the purposes of this paper what happened to the fenestration in these different techniques. One of the Sourdille procedures is a success from both the practical and the audiometric standpoint. The time element in this case since the completion of the final phase of the Sourdille is 18 months. Figure 2 is the audiometric record of this case to date of this report and Figure 3 is the photostatic record of the detailed examinations made for each frequency cycle over the whole period of observation. The study of the bone conduction gives interesting data (Fig. 4).

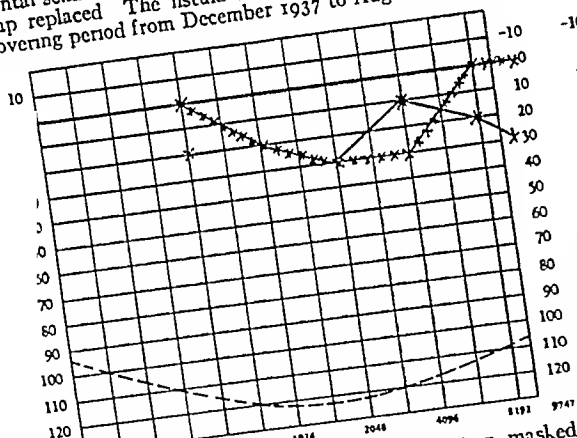
# KOPETZKY OPERATIONS ON LABYRINTHINE CAPSULE FOR OTOSCLEROSIS 479



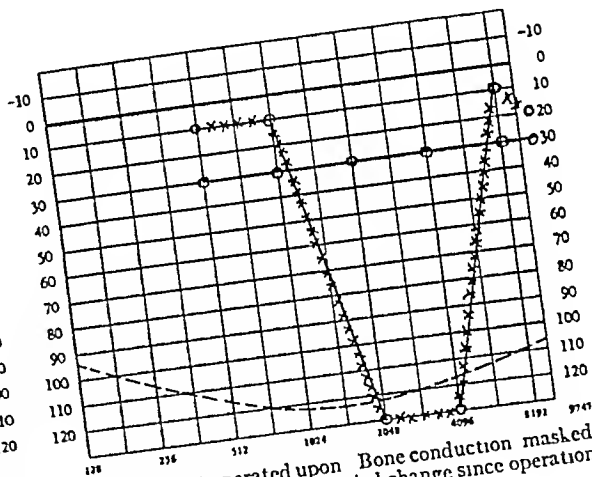
Left ear, not operated upon. Shaded section denotes decibel change since operation, second stage. Starred line indicates postoperative, second stage, curve. At second stage operation, the epidermis was elevated over the horizontal semicircular canal, fenestration performed, and the flap replaced. The fistula remained open during record covering period from December 1937 to August, 1940.



Right ear, not operated upon. The shaded section denotes decibel change since operation, second stage. The starred line indicates postoperative curve.



Left ear, side operated upon. Bone conduction, masked. The shaded section denotes decibel change since operation. The starred line denotes postoperative curve.



Right ear, not operated upon. Bone conduction, masked. The shaded section denotes decibel change since operation. Starred line denotes postoperative curve.

Fig 2 Case of Mrs M C, aged 45. Conventional audiometric charts, showing gain in hearing. The solid line indicates hearing acuity before the second stage of the Sourdille operation. The starred line indicates the last test of hearing acuity. The shaded section below the solid line indicates the level of hearing some time after the first

The other completed Sourdille was a failure. The second Sourdille operation which failed in my opinion, although there is an improvement in the conversational ranges, occurred in a sclerosed type of bone and with a small true cholesteatoma, discovered in the epitympanic space at operation. One of the patients in whom the tympanic structures were left untouched not only has an open reacting fistula 22 months after operation but has

stage. The hearing is improved, in spite of an island of deafness by bone conduction, taken under conditions of masking, with 30 decibels of masking, of same tone as one used in tested ear. The record of conversational losses were, December, 1937, right 58 per cent, left 56 per cent, August 1940, right 55 per cent, left 41 per cent.

hearing sufficiently improved to satisfy the patient. From my objective observations of his audiometric, fork, and voice tests, I would not list the case as a success. The second patient in this group has an open actively reacting fistula after a 19 months' interval of time. The hearing acuity varies with the onset and cession of allergic attacks. Here too there has been improvement in hearing acuity but I do not consider this case a



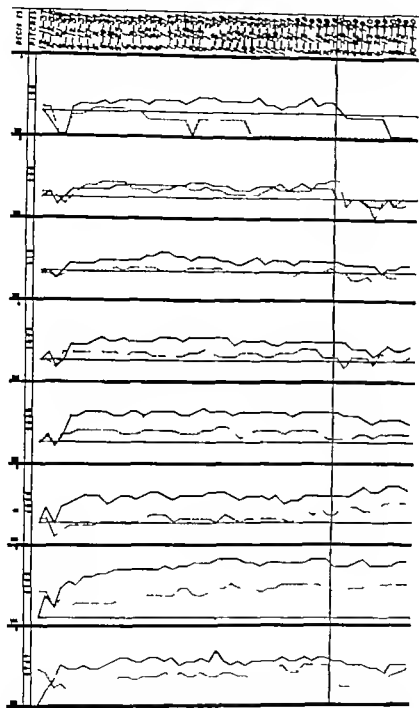


Fig. 5. Case of Mrs M. C., aged 45 years, date of operation, March 30, 1930. Serial record of audiometric tests for air conduction. Shaded area is interval between first and second stage of Soundfile operation. Vertical line indicates change from 6-A to 6-B Western Electric audiometer. There are 49 tests recorded. Closed line indicates ear operated upon. Interrupted line ear not operated upon.

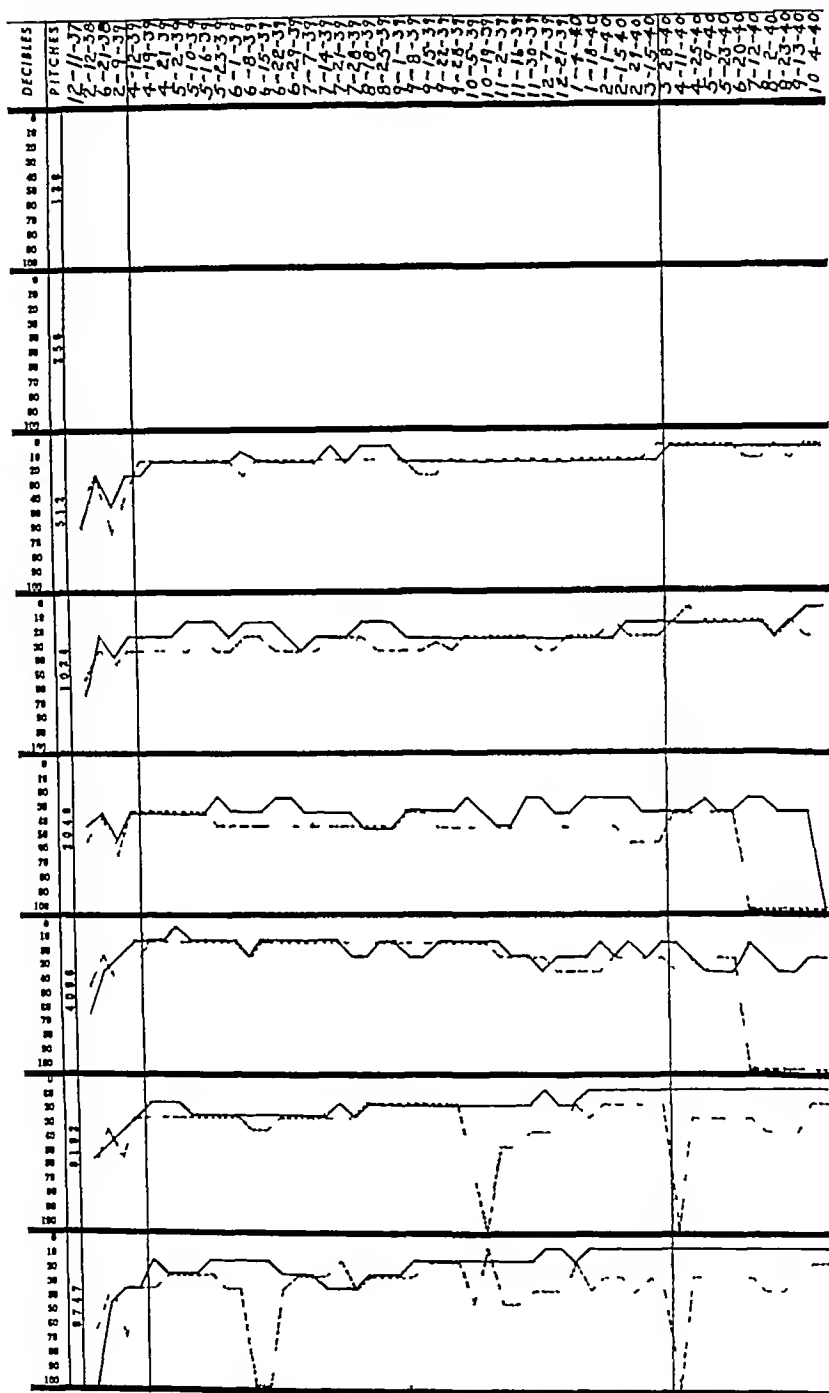


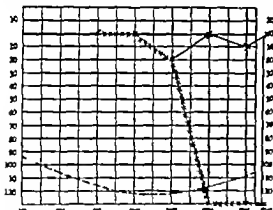
Fig. 4. Same case as in Figures 2 and 3. Serial record of audiometric tests for bone conduction (masked). The dips in bone conduction seem to last about 2 weeks, to be followed by the reappearance of the lost frequency cycle. Repeated tests reveal that the finding is not accidental. The vertical line after March 15, 1940 marks the change from a 6-A to a 6-B Western Electric audiometer.



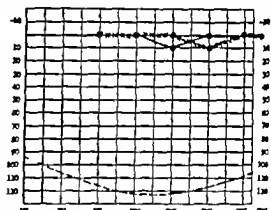
Left ear, operated upon. Shaded section denotes decibel change since operation. Starred line indicates postoperative curve. Fenestration was performed and incus as removed in one stage procedure. Record covers period from February 1939 to September 1940. 1 indicates level of best hearing.



Right ear, not operated upon. Shaded section denotes decibel change since operation. Starred line indicates postoperative curve.



Left ear operated upon. Bone conduction, masked. Shaded section denotes decibel change since operation. Starred line denotes postoperative curve.



Right ear not operated upon. Bone conduction masked. Shaded section denotes decibel change since operation. Starred line indicates postoperative curve.

Fig. 5. Mrs. L. F. aged 47 years. One stage, posttympanic approach. Note loss in bone conduction for upper range of tones. Before blood dyscrasia developed the hearing acuity was better as shown in broken line at 2048 Hz.

blood condition is improving, and patient reports hearing improvement. Record of conversational losses, February 1939, right 5 per cent, left 40 per cent, September 1940, right 5 per cent, left 7 per cent.

successful one. Of the 2 cases in which the epitympanic space was obliterated, head of the malleus amputated, and the incus removed followed by fenestration of the horizontal semicircular canal, one case turned out to be a failure the fistula closed and the hearing acuity did not improve. The other case of this group is a success from every standpoint. The patient had used a hearing aid for many years, is now much improved, and the fenestra is reacting strongly after an interval of 30 months.

Figure 5 herewith presented is the audiometric record of this case. There was a period when the hearing was slightly better than the audiometric record now shows. This is indicated by the broken line on the audiogram. During recent months, this patient has developed a leucopenia, the causation of which is still obscure. The onset of this blood dyscrasia coincides with the drop in hearing acuity. Figure 6 is a photostatic copy of the study in hearing acuity during the whole period. On the bone conduction audiogram

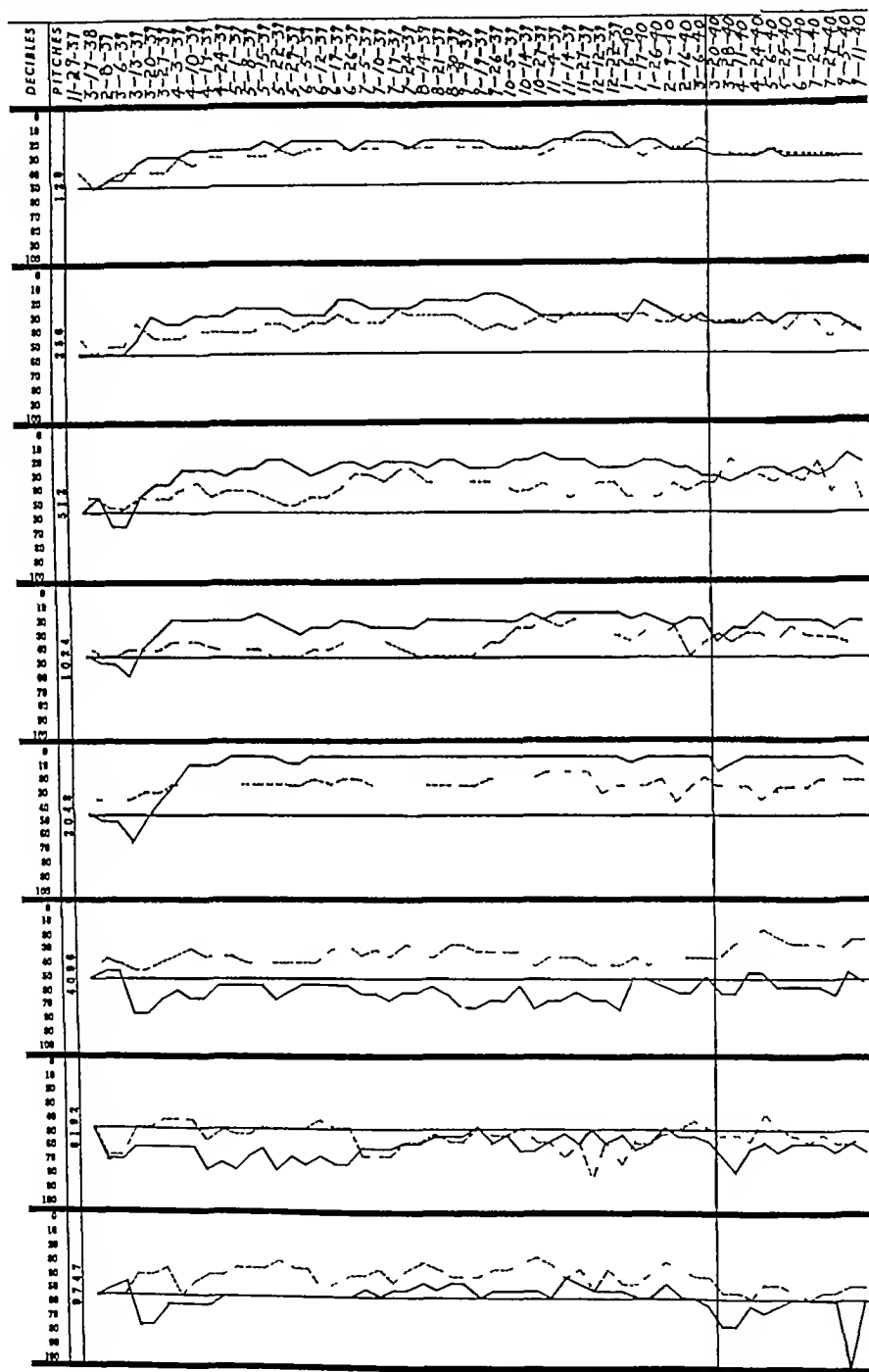


Fig 6 Mrs L F, aged 48 years Operation, February 23, 1939 Work chart, recording hearing acuity over a period from November 29, 1937, to September 11, 1940 There are 55 tests recorded The vertical line indicates a change from a 6-A to 6-B Western Electric audio meter Closed line, ear operated upon, interrupted line, ear not operated upon

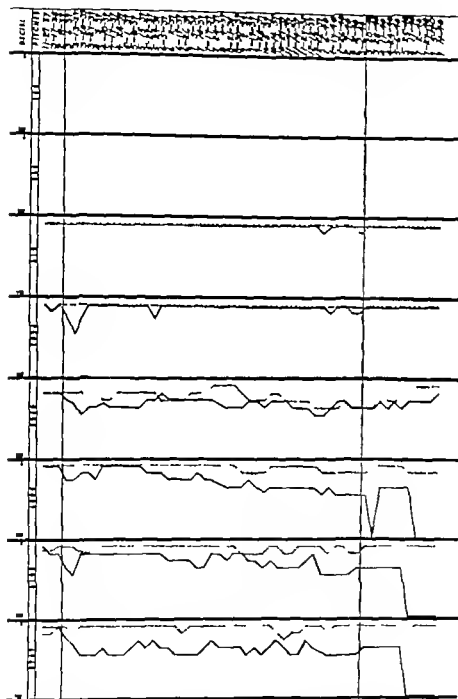
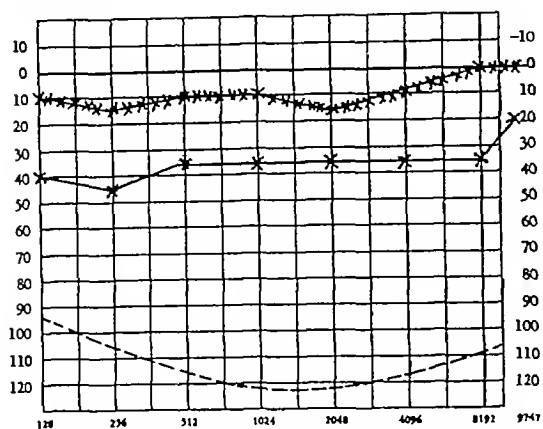
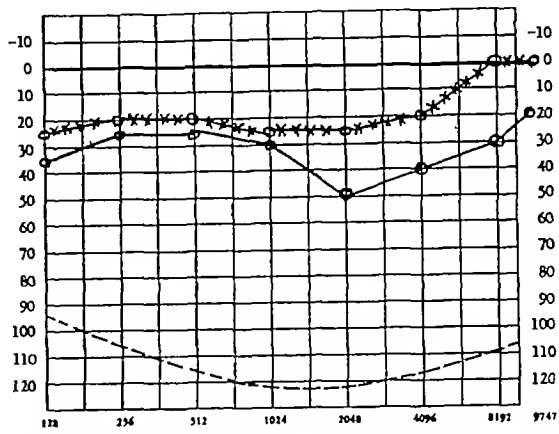


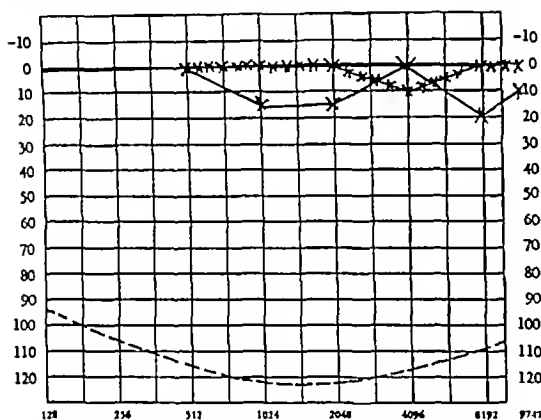
Fig. 7. Same patient as in Figures 5 and 6. Chart of the serial examinations of bone conduction (masked). Change from 6-A to 6-B Western Electric audiometer on March 6, 1930. Drops in bone conduction and subsequent recoveries are unclarified. They are not accidental findings as on days recorded repetition of tests brought same results. Line between February 8 and March 6, 1930, indicates operation. Closed line, operated upon ear; unoperated upon ear; interrupted line.



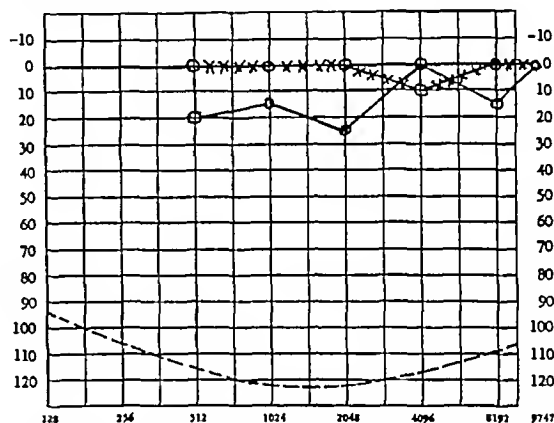
Right ear, operated upon Shaded section denotes decibel gain since operation Starred line indicates postoperative curve



Left ear, not operated upon Shaded section denotes decibel gain since operation Starred line indicates postoperative curve



Right ear, operated upon Bone conduction, masked Shaded section denotes decibel change since operation Starred line denotes postoperative curve.



Left ear, not operated upon Bone conduction, masked Shaded section denotes decibel change since operation Starred line denotes postoperative curve

Fig 8 Miss R. G., aged 24 years Conventional audio metric charts, shaded section shows decibel gain in both ears

Record of conversational losses, October 1938, right 28 per cent, left 28 per cent, July 1940, right, 9 per cent, left, 19 per cent.

(Fig 7) there appear periodically sharp losses in masked bone conduction. Why these occur is not yet clarified. They are not accidental findings because repeated examinations made during these periods always gave similar graphs. Among the 18 operations, all done through the postauricular route, the epitympanic space obliterated, the head of the malleus amputated, the incus kept intact and *in situ* and the horizontal semicircular canal fenestrated, only a very few were sufficiently functionally improved to be listed by me as successful cases. The interval of time since operation

Fenestration of right ear was done and a flap was placed over it. The head of the malleus was removed. For 15 days the flap remained *in situ*. On November 25, 1938, the flap over the fenestration sloughed off. No subsequent covering by flap was done. Record from October, 1938, to July, 1940. Fistula was still open, July, 1940.

is not, in my opinion, sufficient to estimate even the successes. Some of the fistulas are open, with no improved hearing. I shall, of course, report these cases in detail upon another occasion. Here I desire to present the pertinent details of one of these cases which is still a complete success from every standpoint. This is a patient on whom I operated, obliterated the epitympanic space, amputated the head of the malleus, kept the incus intact and *in situ*, and then fenestrated the horizontal semicircular canal. I called attention to this case in my preliminary report because,

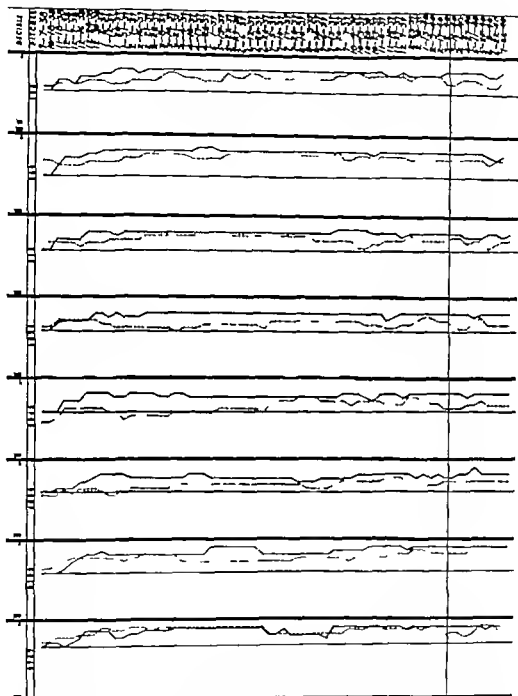


Fig. 9. Miss R. G. Aged 24 years. Operated upon November 8, 1938. Serial audiometric record, showing 64 tests, from September 7, 1938 to July 26, 1940. The critical line indicates change from 6-A to 6-B Western Electric audiometer. A striking parallelism is shown in improved hearing acuity in the ear (broken line) not operated upon.

# KOPETZKY OPERATIONS ON LABYRINTHINE CAPSULE FOR OTOSCLEROSIS 487

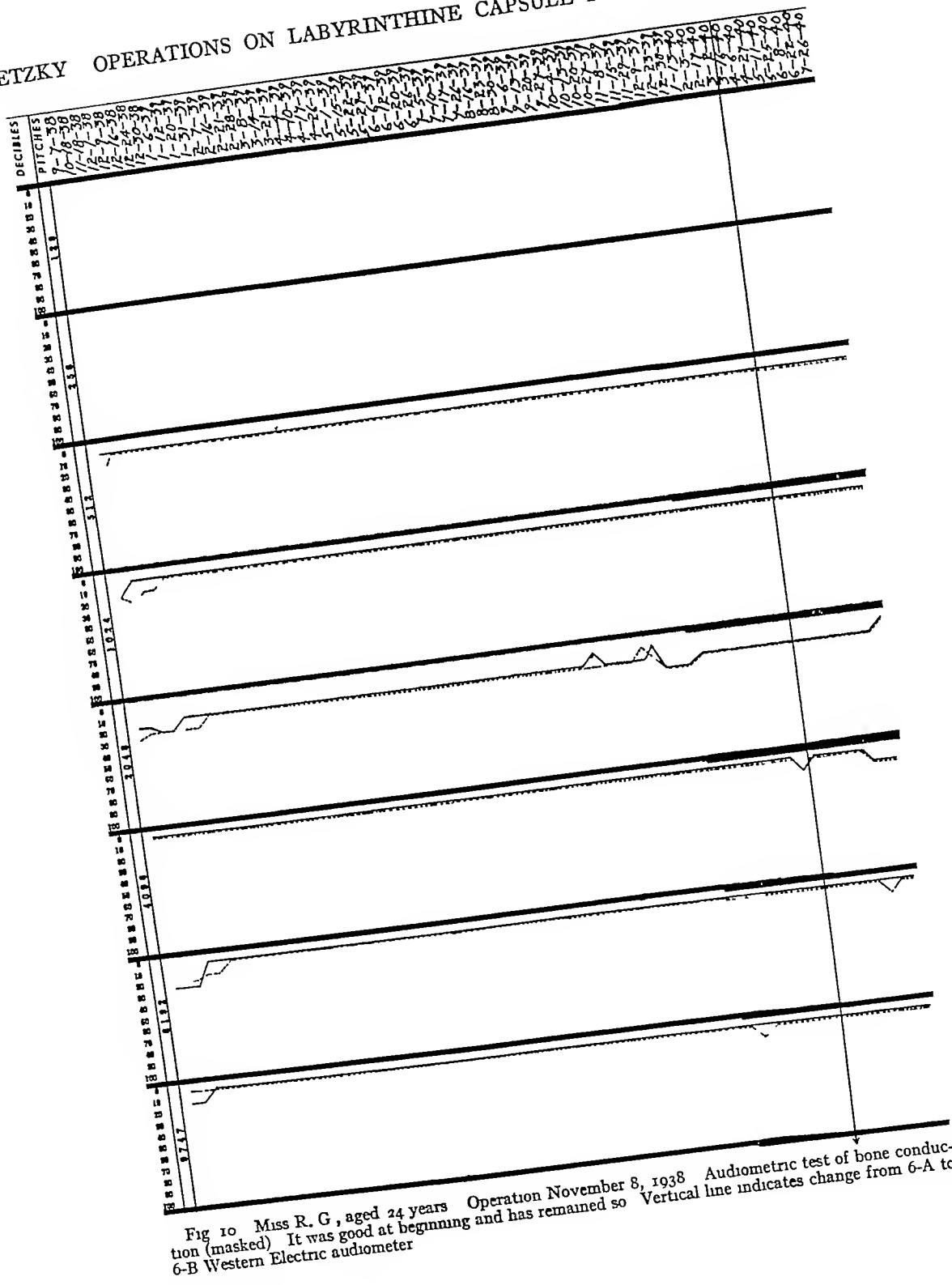


Fig 10 Miss R. G., aged 24 years Operation November 8, 1938 Audiometric test of bone conduction (masked) It was good at beginning and has remained so Vertical line indicates change from 6-A to 6-B Western Electric audiometer



after a very short interval of time the flap covering the fenestra sloughed off. For many months, I kept granulation tissues from growing over the fenestra. After 8 months, when only this area was bare the rest of the wound healed and dry. I permitted the healing to proceed and the coverage of the fenestra became complete. The actively reacting fistula test lessened, upon touch, but is still to be elicited by the Sengle otoscope. The hearing acuity has continued excellent. Figure 8 is the audiometric record of this case to date of this paper. Figure 9 and Figure 10 are photostatic copies of the working charts for the detailed observation of the audiograms of the hearing acuity for each frequency cycle in the scale. The interval of time since operation is 23 months.

#### CONCLUSIONS

In all the patients operated on, the cover of the fenestra has differed, yet closure of the fistula ensued in many but stayed open in some. Had it stayed open always with a given technique and closed with others, I would have discarded all but the technique which always brought success. Unfortunately this could not be done because successes were as scattered as were the failures regardless of the different technical procedures. The majority of the fistulas closed. Yet the ones remaining open seem to substantiate Canfield's and also Guggenheim's experimental results and conclusions, that the closure is less dependent upon the cover material than upon factors and elements inherently present in the bone itself. *The conclusion is inevitable that up to the present no sure way has been devised to make the fenestra and reasonably to expect that it will remain open permanently.*

The successes I have been able to procure in the small amount of clinical material available to me for subsection to operation have been obtained in spite of the different technical procedures performed. *The conclusion is therefore warranted that factors and elements having nothing whatsoever to do with the cover (flap) or with a specific technique are responsible for the results obtained.*

From the manner in which the patients react to the surgery and the end-results from exactly similar technical procedures, with similar audiometric findings, and the usual case histories and otoscopic findings, it is evident that systemic conditions, endocrine and metabolic dysfunctions play a part not only in causing the deafness but in continuing it after fenestration. As a corollary from the observation of the various postoperative periods, the conclusion seems logical that the cases fall into different categories: the exact recognition

and diagnosis of which is not possible at this stage of our knowledge.

Observations of the patients, who have had successful fenestrations and whose hearing from tests by voice, forks, and audiometric tests is sufficiently good to be classified as successful and for whom a sufficient interval of time has elapsed since operation present another factor that needs notation. As the patient emerges from the operation period, the vertigo and nystagmus subside and he is sharply conscious of hearing many sounds of which he was unaware prior to operation. These patients are exceedingly anxious to be cured of their deafness. They spend many hours daily continuously and continually testing themselves. Their family and circle of friends all help in this. After a few months have passed, the awakened interest passes. The newness of the increased hearing acuity has worn off. The patients themselves forget how badly they were handicapped prior to operation. So it is no surprise to have some of these patients appear months after operation showing an open, actively reacting fistula with a very satisfactory audiogram of hearing acuity with a maintenance of the gained hearing, yet dissatisfied because they still are not hearing normally and they miss words at the theater or in the general conversations in social gatherings. In some, this induces a psychotic phase enhanced by a phobia of a recurrence of the deafness. I have observed this tendency in both educated and uneducated patients. The conclusion therefore seems inevitable that the greatest possible care must be exercised in making promises of what will be accomplished by these operations. Many troublesome annoying experiences will be avoided if not only the patient but his family are told exactly what this surgery holds out for him and that it is impossible truthfully to predict results on hearing acuity. In many instances I have put this uncertainty in writing to the patient before accepting him as a subject for operation.

Mr Hall summed the whole matter up rather neatly at a meeting of the Section of Otology of the Royal Society of Medicine in London when he said, as long as the patient was fully aware of the nature of the operation, and the chances of improvement, the question of the justifiability (of the operation) did not enter into the matter more than into any other attempt to advance the science of surgery.

At present, within the framework of recorded experiences with this type of surgery and from my own work in this field, it is impossible to make definite estimate of its value to the patient as a

means to restore hearing in a person suffering from progressive deafness of the conductive type. Good results are on record. The exact determination of what type of case will react best upon being subjected to this surgery is still unclarified. The question of what kind of technique will produce the best results in the shortest time with the least danger to the patient is still unsolved. Inherently this surgery, undertaken with the wonted regard for asepsis and a knowledge of the surgical anatomy embraced in the technique, carries little danger to life and only a slight degree of risk to the labyrinthine structures. The risks to the membranous labyrinth, with a resultant further loss of hearing, are definitely increased by reoperations upon the horizontal semicircular canal in cases in which the first fenestration turned out to be a failure. The implantation of pavement epithelium buried from the external air is to be avoided lest pseudocholesteatomas develop.

This type of surgery should be continued with all safeguards and cautions. There is promise in the advancement of the science of surgery in the evolution of this surgical therapy for the deafened

## BIBLIOGRAPHY

- 1 ALDERTON, H. A. Trephining of the stapedial footplate for otitis media sclerosata. *Tr Am Otol Soc*, 1898, 7 60
- 2 BARANY, R. Collected reprints (Die Indicationen zur Labyrinthoperation). *Acta oto-laryngol.*, 1924, 2
- 3 CAMPBELL, E. H. Experiences with fistulization of the labyrinth in chronic progressive deafness. *Arch Otol*, 1939, 30 689
- 4 CANFIELD, N. Labyrinthine fistulas: report of experiments on the vital response to various methods of producing defects in bone. *Arch. Otol*, 1939, 30 50
- 5 FARACI, G. Importanza acustica e funzionale della mobilizzazione della staffa, risultati di una nuova serie di operazioni. *Arch ital di otol.*, 1899-1900, 9 200
- 6 FLODERUS, B. Contribution au traitement operatoire de l'ankylose de l'etrier. *Nord med Ark.*, 1899, 10 No 13
- 7 FREMEL, F. Demonstration eines weger Otosklerose vor 8 Jahren operierten Patienten. *Monatschr f Ohrenh.*, 1922, 56 552
- 8 GRAY, A. A. Otosclerosis résumé. By the American Otological Society, 1928, 11 487
- 9 GUGGENHEIM, L. K., and GUGGENHEIM, P. Artificial fistula in cases of otosclerosis. *Arch Otol*, 1940, 31 1
- 10 HALL. Discussion on modern surgery of the labyrinth. *Society Proceedings of the Royal Society of Medicine—Section of Otology*. *J Laryngol. & Otol.* 1939, 54 365
- 11 HOLMGREN, G. Zur Chirurgie der Otosklerose. *Acta Oto-laryngol.*, 1936, 24 270-283
- 12 Idem. The surgery of otosclerosis. *Ann Otol, Rhinol & Laryngol.*, 1937, 46 4.
- 13 HOLMGREN, G. Surgical Therapy in Otosclerosis. *The Surgery of the Ear*. Chapt. 17, p 398. New York and London: Thomas Nelson & Sons, 1938
- 14 JENKINS, G. F. Serial microscopic sections of the labyrinth and middle ear showing ankylosis of the stapes, otosclerosis. *Proc Royal Soc Med*, 7 Otol Sect., 40 55 1913
- 15 Idem. Otosclerosis. *Tr Internat Cong Med.*, Sect 16 (Otol.) pt 2 609 1913
- 16 Idem. *Proc Royal Soc. Med*, Sect. of Otol, 1930, 23
- 17 KEND, L. Personal communication. This is another surgeon who is doing labyrinthine fenestration to improve hearing. His cases have not yet been reported. He does not profess to use Shrapnell's membrane, and has successful cases on his records. He employs the postauricular route of approach.
- 18 KESSEL, F. Ueber das Ausschneiden des Trommelfelles und Mobilisieren des Teibugles. *Arch f Ohrenh.*, 1876. Later article 1877
- 19 Idem. Ueber die vordere Tenotomy, Mobilisierung und Extraction des Stapes. *Arch f Ohrenh.*, 1894
- 20 KISCH, H. Presentation before Royal Society of Medicine. *Proc Royal Soc Med*, 1912, 6 36 Sect. Otol.
- 21 Idem. *Proc. Royal Soc. Med*, Sect. of Otol, 1930, 23
- 22 KOPETZKY, S. J. Studies in labyrinthine fenestration to improve hearing (preliminary report). *Laryngoscope*, 1939, 49 1064
- 23 LEMPERT, J. Improvement of hearing in cases of otosclerosis: a new one stage surgical technic. *Arch Otol.*, 1938, 28 42
- 24 Idem. Endaural fenestration of external semicircular canal for restoration of hearing in cases of otosclerosis: summary report of one hundred and twenty cases. *Arch Otol*, 1940, 31 711
- 25 LUCAS, A. Die chronische progressive Schwerhoerigkeit, ihre Erkenntnis und Behandlung. Berlin: F. Springer, 1907
- 26 PASSOW, C. A. In discussion of paper by Panse. *Verhandl. d deutsch otol Gesellsch.*, 1897, 6 141
- 27 SOURDILLE, M. The surgical treatment of otosclerosis. *Proc. Royal Soc Med*, Sect. of Otol, 1930, 23
- 28 Idem. New technique in the surgical treatment of severe and progressive deafness from otosclerosis. *Laryngoscope*, 1937, 42 853-873

# GLAUCOMA SURGERY DURING THE PAST TEN YEARS

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**I**N the management of primary glaucoma the trend is more and more toward earlier operation when indicated. Unfortunately however there is still considerable procrastination on the part of many patients and ophthalmologists, and this is to be regretted in view of the better results obtained from operations on early cases as compared with the results with late cases. In a series of 141 eyes operated upon 90 per cent of the early cases, 51 eyes, showed arrested disease after an average follow-up period of approximately 5 years from operation. Of the late cases, 90 eyes, only 18 per cent showed arrested disease after an average follow-up period of over 5 years from the operation.

In 43 per cent of the advanced cases in this series, the field changes continued to progress in spite of the fact that the operation was successful in reducing the intra-ocular pressure to normal over the 5 year follow up period. This would indicate that if the vascular process occasioned in the retinal vessels by the increased intra-ocular pressure producing the field changes has progressed to a certain point, or has gathered a certain momentum so to speak, it continues to progress, thus producing progressive field defects in spite of normal intra-ocular pressure. There can be small hope, therefore for an operative panacea for primary glaucoma so long as operation is deferred until this vascular process has gathered sufficient momentum to progress regardless of the successful reduction of the intra-ocular pressure.

Conceding that the goal of all glaucoma operations is permanently to reduce the intra-ocular pressure to normal, but bearing in mind that this goal may be attained to no avail if the operation has been deferred too long, we shall proceed with a discussion of trends in operative technique during the past 10 years. These have been largely in the nature of modifications and combinations of our standard procedures (Iri-

dectomy iridectomy with sclerectomy trephine, cyclodialysis, and iris inclusion). It is well to bear in mind that these standard procedures when employed early in the course of the disease in the indicated cases are highly satisfactory in the large majority of instances.

In presenting relatively new techniques very little emphasis will be laid on the statistical claims of their sponsors. In view of the difference in the tractability of the disease to treatment between its early and its late stages, such figures would appear to have little value unless the stage of the disease at which the operation was performed were also known. Clearly it would be unfair to compare the results of one operation done in the early stage with the results of another done when the glaucoma was absolute. The new procedures are usually used sporadically frequently on advanced cases as secondary or tertiary operations, and are often reported in small series which have not been followed up adequately. Such series are not to be compared with the large series available in which long tried techniques have been carried out in the presence of early as well as advanced conditions and which have been followed over a period of years.

Although ophthalmologists agree that an iridectomy is the operation of choice in acute glaucoma and that the other procedures are contra-indicated unless, perhaps, an iris inclusion can be performed during an interval free of tension, opinion regarding other indications for the use of the various operative techniques is so divided that it is impossible to generalize with regard to it. Any tendency toward unanimity of opinion in this matter which appears to have developed in recent years, however will be noted.

## OPERATIVE TECHNIQUES AND MODIFICATIONS

In the fistulizing operations there has been an effort to secure better filtering areas by having a minimum of adhesion between the conjunctiva and the underlying tissue thus a more diffuse and flatter bed is secured and also thicker covering of the filtering area as a protection against ectogenous infection. Contributions to this end have been made by Benedict, Gifford, Berens, and MacMillan.

Benedict advocates a method of dissecting the conjunctival flap which he believes assures a

Early cases were considered those in which the peripheral fields had not contracted to  $\geq$  point closer than 30 degrees of fixation in any meridian and in which the blind spots were not larger than 5 degrees in any diameter. All others were considered advanced cases.

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diffuse, generous, subconjunctival filtration of aqueous, thus avoiding the small, localized, elevated, thinly covered filtering bleb or the flat conjunctival bed with no filtration. He claims that the space between Tenon's capsule and the sclera is a confined, limited one but that the space between the conjunctiva and Tenon's is potentially large and thus the desirable one for filtration. His dissection, therefore, is not subconjunctival but subcapsular in order to avoid adhesions between the conjunctiva and the capsule. This is carried down to within 3 millimeters of the limbus, where Tenon's capsule ends, and from this point to the limbus the conjunctiva is dissected from the underlying sclera just sufficiently to reach the limbus over a wide enough area to permit the placing of the trephine blade.

Gifford has reported on the advantages of the watertight suture of Foster Moore. This is a running, closely placed, continuous silk suture which closes the conjunctival wound tightly, and when it is used the anterior chamber usually reforms on the operating table. The aqueous filters out under the flap, elevating it diffusely, this prevents union with the underlying sclera and thus prevents adhesion. Gifford also attributes choroidal detachment and the rapid constriction of the field of vision following a fistulizing operation to postoperative hypotony and he claims that this condition is the result of a leaky conjunctival wound which may be prevented by the watertight suture.

Berens has devised a specially grooved spatula which he inserts under the tightly sutured conjunctival flap to direct the nozzle of an anterior chamber irrigator in order to bleb-up the flap with one-half normal saline solution.

MacMillan recommends the injection of air under the conjunctival flap as well as in the anterior chamber at the completion of the trephine operation. He accomplishes this with a fine curved lacrimal syringe needle after having placed a continuous watertight suture. The air disappears in about 1 week.

**Trephine.** In the past decade very little has been advanced on the trephine operation. Although there is fairly general agreement that the operation is one of the best operations, if not the best, to reduce intra-ocular pressure, surgeons are more and more seeking other techniques which are better tolerated by the eye and therefore incur fewer complications.

The low-grade chronic iritis that sometimes ensues may be due to the incarceration of ciliary processes in the trephine opening but is really no better understood now than formerly.

The hypotony, which may reach serious proportions, may be corrected by a technique employed by Wheeler, as follows. The epithelium is removed over the upper part of the cornea adjacent to the limbus from 10 to 2 o'clock with a curette. The conjunctiva is incised around the limbus over its upper half and dissected up sufficiently to bring a conjunctival flap down over the denuded cornea, the conjunctiva covering the filtering cicatrix may or may not be excised. The flap is then sutured to the conjunctiva and episclera near the limbus in about the horizontal meridian. If too much of the filtering cicatrix is excised, too large a conjunctival flap will have to be brought down and a slight ptosis may result. This operation is quite effective in raising the intra-ocular pressure to the normal range.

Hans Barkan has advised the use of the Shahan thermophore for hypotony following the trephine operation. He applies it to the filtering bleb for 5 to 10 second periods at a temperature of 165 to 170 degrees four times at intervals of several days.

Glaucoma patients with incipient cataractous changes, either in the periphery with no disturbance of vision or encroaching on the pupillary area with visual disturbance, sometimes show a distressing increase in these cataractous changes after correctly performed glaucoma operations have been done. It is generally conceded that this change is more likely to happen after a trephine operation and less likely to follow the iris inclusion operations.

The trephine operation is also more likely to leave the anterior chamber unrestored for an indefinite length of time and cataractous changes may develop even in an eye with no prior lens changes.

Detachment of the choroid is common after a trephine but is often of no importance. Late infections are always possible. The trend is more and more toward the use of the mechanical trephine of Green.

**Modified Lagrange operations.** Berens has advocated a modified type of Lagrange operation. He dissects a conjunctival flap down to the limbus and shelves the cornea for 1.5 millimeters. With a specially devised broad hollow-ground keratome, an incision is made 1.5 millimeters from the limbus and the wound is enlarged 0.5 millimeters on each side toward the limbus, with scissors. With a specially devised scleral punch the central lip of the wound is serrated. A two cut iridectomy is done, the iris being torn at its root. The conjunctiva is closed with a watertight continuous suture.

and one-half normal saline solution irrigated under the conjunctival flap as described elsewhere.

Lawrence Post advocates a subconjunctival type of incision in performing an iridectomy. The upper half of the conjunctiva is ballooned with an injection of normal saline solution. With a Graefe knife a Lagrange type of incision is made over the upper one fifth of the limbal circumference. The knife emerges under the conjunctiva and is withdrawn without making any more conjunctival opening than the original puncture wound. This is enlarged to 4 millimeters with scissors and the iridectomy is then performed through it.

Spratt dissects down a pocket conjunctival flap, shelves the cornea 1.5 to 2 millimeters, makes a Lagrange type of incision excises a lip of the sclera, and does an iridodialysis by pushing the iris down with forceps toward the pupillary area.

Curdy dissects down a conjunctival flap and excises an elliptical piece of sclera by starting the incision *ab externa* and completing it with scissors.

*Iris inclusion operations:* The usual iris inclusion operations consist of the meridional and transverse types of iridencleisis, with modifications of each and the iridotaxis operation. During the past 10 years several modifications of these procedures have been advanced. Herbert advocates the production of an iridodialysis before pulling the iris out for inclusion according to the iridotaxis technique. He claims the iridodialysis interferes with the blood supply of the included iris sufficiently to cause it to atrophy and disappear in time after it has served its purpose of causing fistulization, and also that over the fistulizing area the conjunctiva thickens and thereby serves as a better protection. The dialysis abrogates the function of the dilator muscles, thus preventing it from pulling the iris back into the eye. Herbert has also recommended the same type of subconjunctival Lagrange incision for performing an iridotaxis as Post has advised for doing an iridectomy.

Greenwood makes a Lagrange incision, excises or punches the scleral lip, does two meridional cuts in the iris, and includes the tongue of iris between these two cuts. The conjunctiva is closed with a watertight suture.

Denig recommends what he terms an iridotorion operation. The included portion of the iris is curled around a wire so that the pigment epithelium is out, thus forming an epithelial-lined tube of iris tissue extending from within the eye out under the conjunctiva.

Goss and Schultz advocate dissecting a conjunctival flap and making a 6 millimeter incision near the limbus with a keratome *ab externa*. A meridional iridotomy is done and one pillar is flattened out along the scleral surface with the pigment layer exposed. Constantine does a similar procedure but includes both pillars.

Gifford advises an iridencleisis with meridional iridotomy as particularly efficacious for buphthalmos, and Wolfe recommends the use of the same type of procedure combined with a sclerectomy as particularly good in the treatment of glaucoma in aphakic eyes.

A considerable number of surgeons feel that the iris inclusion operations should not be done in cases of congestive glaucoma. Massage after the operation is frequently practiced.

*Cyclodialysis:* The question of how the cyclodialysis operation functioned was in dispute for some time. Some claimed that it was due to the passage of aqueous from the anterior chamber directly into the suprachoroidal space; others, that freeing of peripheral synchiae at the time of operation was most important, others, that atrophy of the ciliary body resulting in subnormal aqueous output, was the rationale of the operation.

It has now been definitely established, however, that the operation works because of a fistulous opening from the anterior chamber into the suprachoroidal space. It is also agreed that this fistulous opening tends to close so that the operation leads to a permanent reduction in intra-ocular pressure in only about 20 per cent of unselected cases. Efforts have therefore been directed toward securing a permanent fistulous tract.

Mankach has tried to accomplish this by what might be called an intra-ocular or a suprachoroidal iridotaxis. A technique for ordinary cyclodialysis is carried out except that the scleral opening is made only about 4 millimeters from the limbus and 4 to 5 millimeters wide (Fig. 12). With slightly curved, delicate forceps the iris is grasped via the cyclodialysis route and pulled backward into the suprachoroidal space but not to the scleral opening (Fig. 13 and c). Mankach reported on only 4 eyes operated upon by this method, the tension was reduced in 3 but there was only a short follow-up period. The only other report on this operation that I have been able to locate is one by Saker who employed it on 24 eyes in 13 patients. Tension was reduced in 20 eyes followed from 0 days to 1 month. The fact that in years time there has been no further report, either by the sponsor or others, would seem to indicate that the operation has not proved satisfactory.

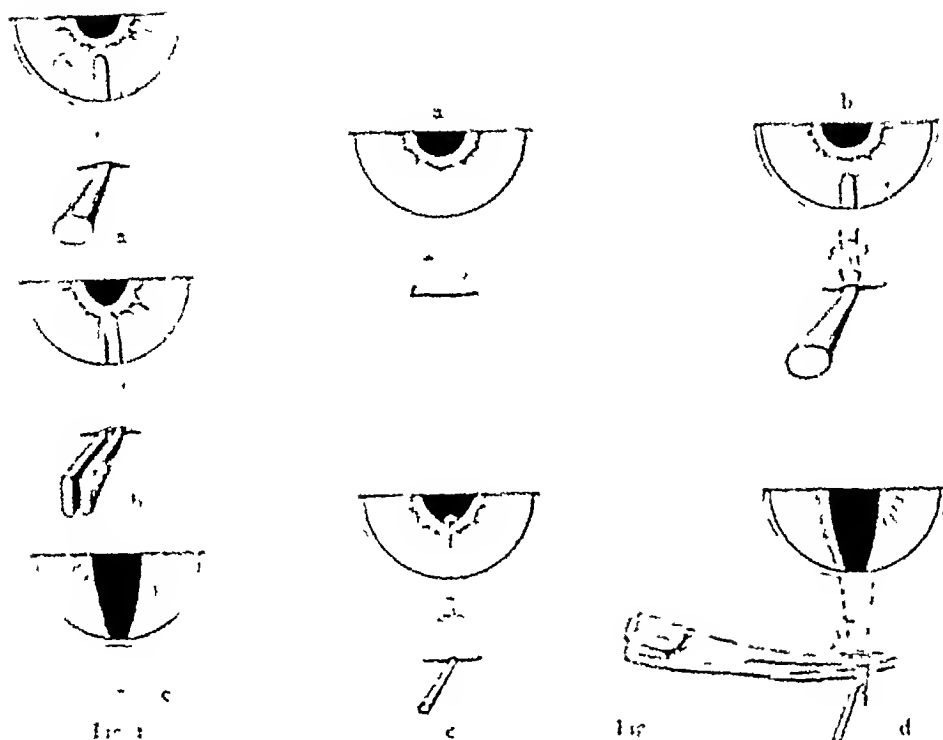


Fig. 1. The Del Barno operation consists of a scleral incision 1 to 2 mm. in diameter, 1 mm. in depth, by the use of a pair of scissors. The incision is made in the sclera, 1 to 2 mm. from the limbus, and the depth is such that the iris is just visible through the opening. The incision is made in the sclera, 1 to 2 mm. from the limbus, and the depth is such that the iris is just visible through the opening.

Fig. 2. The Del Barno operation is completed by the use of a blunt hook to engage the iris and pull it through the external scleral incision. The incision is made in the sclera, 1 to 2 mm. from the limbus, and the depth is such that the iris is just visible through the opening. The incision is made in the sclera, 1 to 2 mm. from the limbus, and the depth is such that the iris is just visible through the opening.

Del Barno has advocated a modification of the Mauk operation. After dissecting a conjunctival flap he makes a keratome incision obliquely through the sclera 3 millimeters from the limbus at 10-30 o'clock for the right eye and at 1-30 o'clock for the left eye. The incision is made quite tangentially, the sclera being traversed over a distance of from 2 to 3 millimeters (Fig. 1a). The internal opening is only just large enough to admit comfortably a spatula which is advanced between the sclera and the ciliary body until it appears in the angle of the anterior chamber (Fig. 1b). The usual cycloablation is then done over as wide an area as possible. After the spatula is withdrawn, a small blunt hook is inserted through the same tract, the pupillary margin is engaged, and the iris is withdrawn until it just emerges through the external scleral incision (Fig. 1c). A small piece of the sphincter is excised to prevent the iris from being drawn back inward and the conjunctiva is closed (Fig. 1d).

This operation is supposed to have certain advantages over the Mauk technique. Forceps are not used to grasp the iris and the incision can therefore be smaller and a tendency toward ectasis of the ciliary body avoided. Also injury to the ciliary body is less likely with the hook. The operation had been performed on 50 patients with good results.

Another technique advanced to keep the communication between the anterior chamber and the suprachoroidal space open is that of Troncoso. This consists of the usual cycloablation procedure supplemented by the implant of a strip of magnesium. This is done by a specially devised instrument which is inserted through the scleral opening along the tract of the cycloablation operation for a short distance into the anterior chamber. The magnesium emits hydrogen gas and disappears in about 20 days. It is nonirritating and the gas prevents a closure of the operative opening as well as the reattachment of the ciliary body.

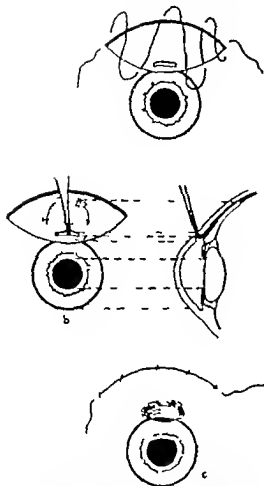


Fig. 5. The Queiroga operation, combination of sclerectomy, anterior cyclodialysis, and peripheral iridectomy. a, Conjunctival incision with continuous silk suture placed. The 3 millimeter sclerectomy is shown. b, The spatula is inserted through the sclerectomy opening into the suprachoroidal space thus severing the scleral spur. c, The peripheral iridectomy and conjunctiva closed.

to the sclera. The technique has been studied extensively on animal eyes and employed on 33 human eyes.

Brecher used the *membrana testacea*, which is the delicate keratogenous membrane just under the shell of an egg, for insertion into the anterior chamber through the tract of the cyclodialysis operation. Only 1 patient had been operated on when the report was made and the follow-up was for a period of only 5 weeks.

A modification of the usual cyclodialysis technique has been advocated by Salimann. This consists of placing a 1.5 millimeter trephine open

ing in the sclera 8 millimeters from the limbus instead of making the usual scleral incision. The author claims that with this technique there is less chance of prolapse of the vitreous and injury to the ciliary body. He also believes that there is a passage of aqueous from the anterior chamber through the trephine opening for about 3 weeks and that this helps to keep patent the cyclodialysis opening through the scleral spur.

Gifford proposes certain departures from the usual technique. He gives 100 cubic centimeters of 50 per cent solution of sorbitol intravenously the night before the operation. Sorbitol has advantages over the other hypertonic solutions by virtue of its more prolonged effect and the fact that it can be used safely in diabetes. The scleral incision is made 3 to 4 millimeters long and the anterior lip is punched out with a Keith punch. After the operation a 0.5 per cent solution of physostigmine is instilled with the idea that the miotic will tend to prevent the forming of adhesions of the iris root to the sclera, and that in this manner closure of the cyclodialysis opening will be avoided.

Whetler has advocated a combination of the cyclodialysis operation with iridectomy. After the cyclodialysis has been performed, a keratome incision is made at the limbus under the conjunctival flap and an iridectomy performed. One of the rationales of this operation is that the cyclodialysis procedure frees any peripheral synechias present and the iridectomy then removes the iris over this area and thus opens up the angle for future drainage and also prevents synechiae from re-forming. It seems quite doubtful, however, whether an angle thus opened is ever able to resume drainage. In any case the operation accomplishes one important thing: i.e., the removal of the iris over the area of the cyclodialysis so that it cannot become adherent to the sclera opposite its recessed site which would close the communication between the anterior chamber and the suprachoroidal space.

Lauber approves of the cyclodialysis combined with iridectomy but prefers to perform the iridectomy first. He makes the scleral incision for the cyclodialysis, then the limbal incision, and performs the iridectomy and then completes the cyclodialysis. Following the trephine operation he sometimes inserts a spatula through the trephine opening and does a cyclodialysis. This is easier to do when a 1 millimeter trephine is used.

Another modification of the cyclodialysis operation is that sponsored by Queiroga. This is a combination of sclerectomy, anterior cyclodialysis, and peripheral iridectomy. The tech-

nique is as follows After a conjunctival flap is dissected down to the limbus above, two parallel horizontal incisions are made partly through the sclera, 1 millimeter apart, 2 millimeters from the limbus, and approximately 3 millimeters long One of the scleral incisions is carried deeper than the other until aqueous appears at one point. The sclera is then grasped with fixation forceps and the 1 by 3 millimeter piece of sclera is excised with scissors (Fig 3a) A spatula, bent almost at right angles, is inserted posteriorly into the filtration angle, through the scleral spur, and into the suprachoroidal space, and is rotated over a dissection angle of 90 degrees (Fig 3b) If peripheral synechiae are present, the spatula is inserted anteriorly and the synechiae freed A peripheral basal iridectomy is then performed (Fig 3c)

This operation is advocated by the author in all types of glaucoma except acute glaucoma and secondary glaucoma from intra-ocular inflammation, or subluxated lens Twenty-one eyes were operated on and the intra-ocular tension was reduced to normal in every case Some of the patients were not followed after their discharge from the hospital, others were followed only several weeks, and none was followed longer than several months

There is fairly general agreement now that the straight cyclodialysis operation is especially indicated in glaucoma secondary to cataract extraction and dissection This has been particularly stressed by Elschnig, Gradle, and Gifford who point out that its effectiveness in this type of glaucoma may be due to the fact that adherent pillars and tags of capsule can be separated from the scar, that, when an iridectomy has been performed, and the spatula is directed especially over the area of the coloboma, the new channel for drainage is more likely to remain open since the iris cannot adhere to the sclera and thus close the new opening, and lastly, that it is the only operation that can be done in this type of case with assurance that vitreous will not be lost Another reason, however, would seem to be that the aphacic state of the eye minus the zonular pull during accommodative effort, which tends toward less apposition of the ciliary body toward the sclera, predisposes to a patent communication between the anterior chamber and the suprachoroidal space

In cases of primary glaucoma the operation is indicated more in the chronic, simple type of case in which the tension is relatively low Any postoperative rise of tension tends to press the ciliary body against the sclera and close the drainage channel

*Seton operations* Two types of Seton operation have been revived Row does the usual cyclodialysis procedure and then inserts a special grooved spatula through the operative tract and passes through this groove a piece of looped horse-hair until the looped end appears in the anterior chamber The two ends which project from the scleral opening are buried under Tenon's capsule the limbus down and in, and another down and out A keratome incision is made into the anterior chamber at the limbus under each flap A straight blunt-tipped lacrimal needle, threaded with braided white silk, is inserted into the anterior chamber from one incision to the other and the needle is withdrawn, thus leaving the thread extending across the anterior chamber Each end is cut off 4 to 5 millimeters from the limbus An advantage claimed for this is that the silk can be manipulated if necessary to restore further drainage Reitsch dissects down a tongue of sclera 1 5 millimeters by 6 millimeters extending through half the thickness of the sclera and having a fixed base at the limbus A keratome incision is made and the tongue of sclera is inserted between the lips of the incision and into the anterior chamber Four patients were operated upon by this method, with good results

*Cyclodialysis punctures* A new principle in the operative treatment of glaucoma has been advanced by Vogt He reports on cyclodialysis punctures which he claims reduce the intra-ocular tension by lessening the production of aqueous The operation is performed by a circular incision in the conjunctiva, 4 to 5 millimeters from the limbus, thus exposing the sclera Sixty to 100 punctures of from 1/2 to 1 second's duration are made with a diathermy needle 0.5 millimeter long and 0.18 to 0.2 millimeter thick to form a girdle zone extending not closer than 2 1/4 to 3 millimeters from the limbus and extending backward 5 to 6 millimeters from the limbus The current used should be 60 to 70 milliamperes There should be good conjunctival closure The further away from the limbus the punctures are made the less deep they should be On the grounds that the physiological production of aqueous is too much for a glaucomatous eye, this operation seeks to reduce this production to subnormal by injury to the ciliary body When the operation has been successfully performed even the use of homatropine and atropine fails to produce a rise in tension The author admits that the inability to regulate the effects or dose of the operation is a disadvantage



The complications of the operation, which arise principally as a result of making the punctures too close to the limbus and of not having the needle the proper size, are as follows: (1) marginal keratitis which occasionally progresses to ulceration; (2) cataract which is particularly prone to develop if incipient changes were already present; (3) iritis with posterior synechiae; and (4) iris and anterior chamber hemorrhage which may appear as late as 8 to 14 days postoperatively.

Vogt feels that the operation is not a serious competitor of the customary procedures for increasing the aqueous outflow because of the tendency to complications. It is to be used primarily when other methods have failed particularly in the following types of cases: (1) total and long standing absence of the anterior chamber especially in those cases in which the anterior chamber fails to re-form and the tension remains elevated after an operation; the author reports on the results of this technique in 5 such patients; the tension was reduced to normal and the anterior chamber re-formed; (2) glaucoma in aphasic eyes, especially when there is vitreous in the anterior chamber; (3) glaucoma with cataract, in preparation for the cataract extraction; (4) hemorrhagic glaucoma, and (5) iridocyclitis with secondary glaucoma. The inclusion of this last type is surprising but Vogt has performed this operation on several such patients with resultant normalization of the tension; most amazing of all, the corneal precipitates disappeared.

Lloyd has been successful in reducing intraocular pressure by the application of diathermy heat alone.

**Vitreous fistula operations.** Lindner has reported an operation designed to produce a vitreous fistula by means of the following technique. At a site down and out, a triangular conjunctival flap is dissected up with the apex at the limbus 10 millimeters from the limbus; a 2 millimeter trephine is done through one half the scleral thickness, and this portion of the sclera is removed; electrocoagulation is applied to the base and the walls of the trephine opening with the idea of coagulating the adjacent choroid and retina; then a 1½ millimeter trephine opening is made through the base of the former trephine site; the exposed choroid is punctured with a dissection needle; a bead of vitreous presents, and, by light pressure on the globe and by sticking the dissection needle deeper another bead presents and is cut away; this should be repeated until fluid vitreous appears; the conjunctiva is then closed.

This operation is indicated in cases of glaucoma with very high tension (80 to 100 Schlotz) and

almost no anterior chamber and in cases in which the anterior chamber does not re-form for a long period following a glaucoma operation. It is a transitory fistulization which contracts the vitreous and re-establishes or deepens the anterior chamber and is to be looked upon only as a rescue measure to make a later operation easier and safer. The author has performed the operation on 50 eyes with only 1 complication. This was a retinal detachment which occurred because of insufficient coagulation and which was later successfully re-attached.

**Goniotomy and multiple iridectomies.** Otto Barkan divides cases of primary glaucoma into two groups as follows:

1. Deep chamber glaucoma. This is characterized by an anterior chamber of usual depth and by an open filtration angle. The underlying pathology is an obstruction in the sclerocorneal trabeculae which induces a retention glaucoma and suggests for this group the term "trabecular glaucoma." In this group are the cases usually referred to as chronic simple glaucoma, chronic noncongestive glaucoma, and senile glaucoma, and for the early cases he recommends primarily the operation of goniotomy according to the following technique. The operator wears a binocular head loupe. The patient's pupil is previously contracted with eserine. A specially devised contact glass is inserted which affords a magnified view of the interior of the filtration angle. A special goniotomy knife is passed across the anterior chamber and through the optic axis to the opposite angle and an incision is made in the trabeculae for one-fourth of their circumference. According to the author this re-establishes the normal direction of outflow from the anterior chamber into the canal.

Goniotomy is advocated in early trabecular glaucoma, which shows a pigment band over the site of the trabeculae, as seen with the gonioscope, indicating mechanical obstruction. In "trabecular glaucoma" with considerable loss of field vision, or with the constriction close to fixation, Barkan recommends one of the internal or external filter ing operations.

2. Shallow chamber glaucoma. This is characterized by a shallow anterior chamber, permeable sclerocorneal trabeculae and a narrow angle, the temporary closure of which produces transitory rises in pressure. In this group are the cases usually referred to as chronic congestive glaucoma and for them he recommends his technique of multiple peripheral iridectomies, performed through multiple valve-like keratome incision as follows. The anterior chamber is deepened

by the injection of physiological saline solution, preceded usually by a posterior sclerotomy and rarely by aspiration of 5 cubic centimeter of vitreous when the vitreous is of firm consistency or has a very high pressure. Several small oblique valve-like keratome incisions are then made at the limbus. Through each of these a small portion of the root of the iris is excised. The author's claim for this operation is that the iridectomies cause a retroplacement of the iris diaphragm over and adjacent to the operative sites, thereby deepening the anterior chamber and widening the entrance or access to the angle.

*Venous communication operation.* Some thought has been given to the possibility that a sclerosis of the sclera causing a constriction of the vortex veins and thus an embarrassment of the vortex return from the eye might be an etiological factor in primary glaucoma. With this in mind Sondermann has suggested an operation designed to establish a communication between the veins of the uvea and the veins of the conjunctiva. With a special spatula-like knife he makes a canal in the sclera which is 2 to 2½ millimeters wide and extends down to the suprachoroidal space. Into this canal Sondermann inserts a narrow strip of conjunctival tissue.

# CONCLUSION

In conclusion, then, it can be said that the trend is more and more toward the early recognition of glaucoma both by the patient and by the doctor. To this end the sight-conservation organizations should make an effort to familiarize the public with the cardinal symptoms of the disease, the doctor should always be glaucoma conscious and detect the disease in its early stages by means of refinements in perimetry, routine use of the tonometer, study of diurnal tension curves, and sometimes by provocative tests. When recognized in its prodromal or early stages it can be treated satisfactorily in a much higher percentage of cases than is possible in later stages, either by non-surgical means or by surgical measures when these are indicated. Ideally, glaucoma should be treated by removing its underlying cause but until this is possible our hope is to prevent, in so far as possible, its deleterious effects by medication or operation. The struggle continues, therefore, to devise an operative technique that is most likely to reduce the intra-ocular pressure to normal and that predisposes to a minimum of complications. It must always be borne in mind, however, that this goal may be attained to no avail if the operation is performed too late in the course of the disease.

# BIBLIOGRAPHY

1. BARKAN, H. Use of Shahan thermophore in hypotony of the eyeball as a result of Elliot trephining operation. *Am J Ophth*, 1940, 23 692-693.
2. BARKAN, O. Technic of goniotomy. *Arch Ophth*, 1938, 12 217-223.
3. Idem. Glaucoma classification, causes and surgical control. Results of microgonioscopic research. *Am J Ophth*, 1938, 21 1099-1113.
4. BENEDICT, W. L. Sclerocorneal trephining. *Tr Am M Ass, Eye Section*, 1940.
5. BERENS, C. History of iridocyclotomy operations. *Am J Ophth*, 1936, Series 3, Vol 19.
6. BRECHER, I. Ueber eine neue Modifikation der Zyklotomie. *Klin Monatsbl f Augenheilk*, 1936, 21 235-237.
7. CONSTANTINE, K. W. Lundsgaard's modification of Holth's iridencleisis. *Am J Ophth*, 1937, 20 728-730.
8. CURDY, R. J. Subconjunctival Lagrange sclerectomy ab externo. *Arch Ophth*, 1940, 23 1173-1174.
9. DEL BARRIO, A. La fistulization interne par l'iridencleisis sclero-ciliaire dans le glaucome. *Ann d'ocul*, 1934, 171 977-998.
10. DENT, R. Die Indotorsion im Vergleich mit der Trepanation, der Lagrangescher Operation und der Zyklotomie. *Klin Monatsbl f Augenheilk*, 1937, 64 1-8.
11. GIFFORD, S. R. Treatment of secondary glaucoma. *Arch Ophth*, 1940, 23 301-315.
12. Idem. Iridencleisis with water tight closure of the conjunctiva. *Tr Am Acad Ophth & Oto Laryngol*, 1927, p 117-128.
13. Idem. Iridencleisis in buphthalmos. *Arch Ophth*, 1934, 11 751-756.
14. GOAR, E. L., and SCHULTZ, J. F. Iridencleisis in glaucoma. *Arch Ophth*, 1939, 22 1035-1045.
15. GREEN, A. S. A new automatic trephine. *Arch Ophth*, 1931, 6 752-753.
16. GREENWOOD, A. Combined iridencleisis and sclerectomy for chronic glaucoma. *Am J Ophth*, 1930, 13 301-303.
17. HERBERT, H. An iris inclusion operation. *Tr Ophth Soc U Kingdom*, 1926, 46 326-332.
18. Idem. The future of iris-inclusion in glaucoma. *Brit J Ophth*, 1930, 15 433-448.
19. Idem. Supplementary note on iris-inclusion for chronic glaucoma. *Brit J Ophth*, 1934, 18 142-148.
20. LAUBER, H. Combined operations for glaucoma. *Tr Ophth Soc U Kingdom*, 1939, 59 267-274.
21. LENDNER, K. Ueber die Anlegung einer Glaskörperfistel. *Ztschr f Augenh*, 1937, 93 117.
22. LLOYD, J. P. F. The treatment of increased ocular tension. *Tr Ophth Soc U Kingdom*, 1939, 59 181-191.
23. MACMILLAN, J. A. Injection of air as factor in maintaining filtration after corneal scleral trephining in glaucoma. *Arch Ophth*, 1939, 22 968-73.
24. MAUKSCH, H. Ein Vorschlag fuer eine neue Glaukomaoperation. *Ztschr f Augenh*, 1929, 67 313-322.
25. POST, L. Subconjunctival iridectomy for glaucoma. *Am J Ophth*, 1930, 13 21-23.
26. QUEIROGA, A. Iridocyclotomy with anterior cyclo-dialysis for glaucoma. Thesis presented for doctor's degree to the Faculty of Medicine University of Minas Geraes Bello Horizonte Brazil June 1939.

27. REESE, A. B. The aim of early operation in chronic primary glaucoma. *Am. J. Ophth.* 1936, 3, 304-306.
28. REITZEL, W. Sclerostichsis (insertion of scleral flap into corneal slit). *Klin. Monatsbl. f. Augenheilk.* 1930, 93, 326-327.
29. ROW, H. Operation to control glaucoma (preliminary report). *Arch. Ophth.*, 1934, 3, 5-19.
30. SALLMANN, L. Die Trepanationszyklodialisoperation. *Zeitschr. f. Augenheilk.*, 1935, 86.
31. SONDERMANN, R. Eine neue Glaukomoperation. *Klin. Monatsbl. f. Augenheilk.*, 1934, 93, 27-30.
32. SPRETT, C. N. Pocket-flap sclerecto-iridodialis in treatment glaucoma. *J. Am. M. Ass.* 1934, 64, 65-69.
33. STENZ, O. F. The filtration operation of Minkuck for chronic glaucoma with preliminary report on 24 operations. *Am. J. Ophth.*, 1935, 14, 732-733.
34. TACONOSO, M. U. Cyclodalysis (th insertion of metal implant in treatment of glaucoma, Preliminary report. *Arch. Ophth.*, 1930, 3, 270-300.
35. VOGT, A. Ergebnisse der Dialthermischebehandlung des Corpus ciliare (Zyklodialisthermischebehandlung) gegen Glaucoma. *Klin. Monatsbl. f. Augenheilk.*, 1937, 90, 9-5.
36. WACKER, J. M. Iridectomy (th cyclodalysis for reduction of ocular tension. *Arch. Ophth.* 1936, 6, 569-572.
37. WOLFE, O. Iridectomy for glaucoma (th apical. *Am. J. Ophth.* 1935, 14, 769-771.
38. WOLFE, O. R., and BLANKS, M. J. Sclerotomy in glaucoma. *Am. J. Ophth.* 1936, 9, 400-405.

# ADVANCES OF THE PAST TEN YEARS IN RETINAL DETACHMENT SURGERY

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EVERY ophthalmic surgeon is familiar with the thrilling and dramatic story of the evolution of the modern operations for retinal detachment. It is unnecessary now to discuss the cruel, barbaric, hopeless treatment of this condition in the pre-Gonin days. Those who are interested in the historical phase of this subject should read W. E. Krewson's article on the "History of the Surgical Treatment of Retinal Separation," from which I have freely borrowed. One will find here descriptions of scleral puncture, aspiration of subretinal fluid, galvanocautery punctures, dissection of the vitreous, longitudinal incisions, sutures of the retina, subconjunctival injections, intra-ocular injections of iodine, electrolysis, Deutschmann's operation and a host of other procedures. The fact that such a vast number of operative measures had been advocated indicates their uselessness.

One should pause here to pay tribute to the man above all others responsible for the modern surgical treatment of retinal detachment. Jules Gonin laid the foundation of his epoch-making discovery of the importance of the tear or hole throughout 17 years of eating, sleeping, and pondering over retinal detachment, as a study of his early writings show. In 1921 he presented his work to a world, which remained skeptical for 8 or 9 years, then followed a deluge of world-wide reports of successful cures of a hitherto practically hopeless condition. This brings us to 10 years ago and the further advances of retinal detachment surgery fall within the scope of this paper. I am reluctant, however, to dismiss Gonin without saying a little more. I had the unforgettable privilege of spending 2 weeks at Lausanne in 1930 and of observing the man and his work. Dynamic, friendly, pink and white, enthusiastic, bubbling and exploding with energy, he laid the wealth of his material and technique before spectators from all over the world, without reservation or stint. His amazing linguistic powers enabled him to explain his ideas in French, German, English, Spanish, Lithuanian, and Portuguese, perhaps other languages too. But one did not need to understand his words, his deeds spoke for

themselves. Since then, of course, the tribute of his colleagues and thanks of countless patients everywhere have been heaped upon his memory and will continue to be as long as ophthalmology exists.

On the flyleaf of my copy of his book, published in 1934, he wrote "post pessimissimum spes nova!", a motto which put a period to his work. He died in June, 1935, and was awarded posthumously the von Graefe medal, one of the most cherished prizes in ophthalmology.

The classical Gonin operation has been replaced, at least for the time being and for the most part, by other procedures. This was done because of certain disadvantages of the operation. These are (Duke Elder) (1) the difficulty in accurate localization of the hole, a *sine qua non* of a successful Gonin operation, (2) the necessity of several operations if localization has not been accurate or if several holes exist, (3) the destruction of the surrounding region of the retina, leading to further hole formation, and therefore, to possible recurrences, (4) the danger of postoperative hemorrhage, with the resultant gross diminution of visual recovery, (5) the formation of vitreous bands at a later date involving traction on and tearing of the retina, with a recurrence of the detachment. However, in spite of these disadvantages, an occasional case presents itself in which the Gonin operation may be the one of choice. I refer here to that healthy patient in whom the hole is recent, single, and not too large in a flat detachment, in a favorable location capable of being accurately localized. In this event, it will be found that the trauma and reaction of the operation are slight, and the recovery and convalescence of the patient materially shortened.

Because of the disadvantages and shortcomings of the Gonin operation, especially the necessity of an exact localization of the hole, other operations have been evolved, none of which is completely satisfactory in every case. At the present time we are in a state of fermentation or flux regarding these operations, but as the evolution continues one can prophesy with confidence that the time is not too far distant when one can predict a successful outcome in 90 per cent of the cases.

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Whatever technique has been promoted, the fundamental purpose of the operation is the obliteration or isolation of the tear or holes of the retina. Gonin's chief contribution was the recognition of the fact that single or multiple tears can almost always be found in every case if searched for long enough, and the cure can only be obtained by sealing it off, by producing an inflammatory adhesive choroiditis.

In the past 10 years then advances in the surgical treatment of retinal detachment have been concerned with the satisfactory solution of the fundamental conditions. These are (1) the finding of the retinal hole (2) its localization, (3) its obliteration, (4) the postoperative and convalescent care of the patient.

*The finding of the retinal hole.* One can do no better, when discussing this topic, than to repeat Duke Elder's words. "The first essential is, then, to find and localize the retinal tear, and this is frequently no easy thing to do. It involves the careful and repeated examination of every part of the fundus under full mydriasis, and since most holes (about 80%) are near the ora, particular attention should be paid to the periphery. Further, since more than one hole frequently exists, the finding of one does not justify the cessation of the search. Small holes in the main part of the fundus are best seen by direct ophthalmoscopy; but, owing to the prismatic effect of the condensing lens, the indirect method allows of easier and fuller access in the extreme periphery. If a hole cannot be seen at a first examination, it may well be hidden by some retinal fold and may be evident after the patient has been kept recumbent for some days, when the configuration of the detachment has changed, or it may be legitimate finally to draw off the interretinal fluid by a syringe with the same end in view.

With regard to the hole itself it need not necessarily be found at the site of the detachment at the time of the examination, for particularly if the hole is in the upper part of the retina, the interretinal fluid may have drained away by gravity to the lower quadrants of the globe inducing an inferior detachment and leaving the hole in an area of flat retina marking the original position of the detachment. Some help in its location may be obtained from the patient's history for he may indicate the initial position of a loss of field, or the appreciation of a black spot, or flashes of light in a definite direction. The proximity of a focus of old choroiditis or areas of recent hemorrhage is frequently a useful guide and the use of red-free light is helpful, since a greater contrast is obtained when the free edges

of the opaque retina are accentuated against the black choroid. Holes in the extreme periphery may be disclosed by transillumination.

*Localization of the tear.* In spite of many schemes and plans advanced to localize the tear more accurately and with more scientific precision the original Gonin method has remained in favor supplemented by a few simple procedures applied at the time of operation. Many authors, hoping to obtain more precision, have calculated the distance and direction of the tear by angular measures and tables of concordances some utilized the perimeter and concave mirror (Dor Dupuy Detempe et al.) others, the perimeter combined with the direct ophthalmoscope (Geist, Lindner). We've used an eye of substitution. Stine advocated the perimetric method with conventional tables of his own devising. Because these methods at their best are not infallible and at their worst, time consuming and difficult, they have been largely abandoned. The present and sufficiently accurate method used by many surgeons consists of an estimation of the direction and distance of the tear by Gonin's method, repeated several times. This is done prior to the operation. When the sclera over the area involved is denuded, a more accurate attempt is made by transillumination, using Arruga's speculum, and various forms of transilluminators. That devised by Lancaster is satisfactory. A preliminary diathermy needle puncture or an electrolysis puncture can be made. The white area of the former or the bubbles in the latter in relationship to the hole can be seen with the direct ophthalmoscope, and the hole accurately localized.

*The production of adhesive choroiditis.* In 1931 Geist and later Lindner used caustic potash applied to the choroid exposed by a series of trephine holes (1.5 mm.) which penetrated the sclera only. Because of the tediousness and difficulty as well as the danger of vitreous hemorrhage due to perforation of a large choroidal vessel, the development of postoperative uveitis and the danger of thrombosis of a vortex vein this operation has been largely abandoned.

The year 1932 saw the introduction of diathermy coagulation for retinal detachment. Larson reported his method of surface coagulation applied to the entire quadrant above the separation eliminating the precise localization of the tear a feature which appealed to many. The positive electrode was a 2 millimeter ball applied to the sclera over the detachment in many places, the contact lasting 3 to 6 seconds producing a parchment like sclera. The subretinal fluid was then drained by one or two trephine openings.

The year 1932 also saw the advent of Weve's operation which combined surface coagulation with multiple micropunctures. He later abandoned the surface coagulation.

In the same year Coppez suggested the use of a pyrometric electrode devised by him. As related by Krewson, "The circuit used by him consisted of two wires of different metals (copper and constantan) soldered at their ends, and a current was generated which varied in intensity, depending on the difference in temperature of the ends of the wires. One soldered end was kept at 0 degrees centigrade and the other acted as the electrode. The degree of heat obtained in the Coppez placed his electrode, a flat disc 2.5 millimeters in diameter, on the sclera a number of times for 20 or 30 seconds until a temperature of 80 degrees centigrade was recorded by the galvanometer. He did not establish drainage until the end of the operation."

Again in the same year Šafář demonstrated his insulated pins or "nails" of iridioplatinum, 1.5 to 2 millimeters long, single or combined into brushes. These were applied as a barrage around the tear and separation by means of a special pair of forceps, and left in place until the entire number was inserted. The advantage of this method was that the subretinal fluid was not allowed to escape until after the operation was completed, thus a soft eyeball was avoided, and a subsequent puncture or trephine was not necessary.

Walker's contribution was a modification of the Šafář nails or brushes replacing these with shorter micropins, and the design of a delicate special high frequency apparatus, which is the one most commonly used at least in the United States. The micropins are inserted about 2 millimeters apart and a current of 25 to 30 milliamperes are used.

From 1932 to the present a constant search was being made by ophthalmic surgeons throughout the world to obtain more satisfactory results with less trauma. Vogt and Imre in 1934 introduced electrolysis, which had already been used by Verhoeff in 1917, and others before him towards the end of the nineteenth century. According to Krewson, Vogt used a galvanic current of 0.5 to 1 milliampere and a long thin steel needle as the cathode or negative pole. The anode consisted of an electrode in the form of a small ball or plate held in contact with the eye. The needle was introduced through the sclera and choroid and withdrawn rapidly. This procedure produces coagulation in the choroid due to the

liberation of anions at the anode, as shown by the presence of free hydrogen bubbles. Recent advocates of electrolysis are inclined to use somewhat higher currents. Gradle (1936) uses about 3, and Moore seldom less than 5 milliamperes. It is Walker's first choice of operation.

The three methods therefore used in the modern operation are (1) diathermy coagulation, (2) electrolysis, (3) surface coagulation. The invention of new instruments and methods of applying them continues apace. Arruga especially has been fertile along these lines, devising tiny threaded plugs to close the trephine openings in cases of perforation of the choroid, lancets for orientation, and a retractor. The last is invaluable. Strampelli's "diathermophanoscope" embodies what is probably a useful idea. It is briefly, a transilluminator and diathermy handle all in one. Meesmann modified Coppez pyrometric electrode, by employing a fine pointed pyrometric electrode in a curved quartz tube with changeable point. Langdon uses the Shahan thermophore at a temperature of 65 degrees centigrade for 1 minute to produce surface coagulation. Gradle and Meyers (1938) and others have devised various electrodes particularly suitable for surgery around the macular area. The LaCarnière electrodiaphane, with which I am sure you are all familiar, has enjoyed a wide and justifiable reputation. The bent and beveled glass tube containing the platinum wire electrode permits the instrument to be applied beneath muscles and behind the globe. The bipolar electrolytic instrument introduced by Von Szily and Machermer in 1936 and described in detail in the *Traité d'Ophthalmologie* by Veil and Dollfus offers many advantages to the use of the usual electrodes. I do not know if they can be obtained in this country.

Each of the three methods of surgical treatment has its ardent advocates. The trend, however, is away from the exclusive use of a single method, and most surgeons are now using a combination of diathermy, electrolysis, and surface coagulation. As time goes on and reports come in, our knowledge will increase and one can readily foresee a standard operation evolved. Both Walker and Peter, for example, use electrolysis to supplement diathermy in the closing of small tears and to reduce to a minimum hemorrhage from retinal vessels. They use it in macular holes and to visualize the correctness of the location of the tear (ophthalmoscopic study). Diathermy puncture is now of two types, the juxtachoroidal and the perforating. The needles are becoming finer and shorter. Juxtachoroidal punctures are

used to isolate the tear by a barrage over the area of separation, the perforating punctures are used to attack the tear itself. The increasing tendency is to operate under the direct control of the ophthalmoscope. A few punctures are made and then the result noted with the ophthalmoscope. A few more punctures, then observation and so on. It therefore is obvious that drugs which will cloud the cornea should not be employed. Surface coagulation, according to Peter is indicated to create a sufficient number of points of choroiditic adhesive spots throughout the separated area.

To summarize briefly, the modern trend of the operation is as follows. The tear or hole is localized as accurately as possible and a surface mark placed on the sclera with diathermy. The localization is verified by transillumination either applied to the sclera and observed with the ophthalmoscope, or by shining the light from the ophthalmoscope through the pupil in the direction of the tear and noting a spot of light on the sclera. The hole is further localized by the insertion of an electrolysis needle or perforating diathermy needle and its appearance noted with the ophthalmoscope. The tear is then surrounded by perforating diathermy punctures, except in the macular area. The needles are introduced and left in place until the entire area of the separation has been treated by surface coagulation and electrolysis, or juxta choroidal diathermy punctures. Some surgeons (Peter) prefer to cover the entire area with negative galvanic needles ( $\frac{3}{4}$  to  $\frac{1}{4}$  mm.) of perforation, and in addition use catholysis freely in the region of the tears. I am inclined to agree with Weve, however, that it is unnecessary to do more than seal off the tear. Insertion of pins over the entire area of the separation except where there is not a hole found is, to my mind, unnecessary mutilation.

It is perhaps pertinent to mention here another operation which may be found to be useful in cases not suitable for the above operations. I refer to the sclerectomy of Mueller modified by Lindner under the term of eyeball shortening operation. This operation is described and illustrated by Fischel and Miller who report a successful outcome in what otherwise probably would have been a hopeless case. It consists of an elliptic excision of a piece of sclera over the detached area, great care being taken not to injure the choroid. A case of retinal detachment associated with a scleral ectasia was successfully

treated by me. The entire staphyloma was excised more or less according to Mueller's technique. I am convinced that no other operation would have succeeded in this case.

**Anesthesia.** Local anesthesia is unsatisfactory. It should be used only when other methods are contra indicated. Avertin anesthesia is the one of choice. If it can be safely used. Its advantages are (1) perfect anesthesia (2) a free field for operating unhindered by the anesthetist, (3) slight danger of postoperative nausea, (4) no disturbance of the conjunctiva and cornea as is caused by local anesthesia, (5) no risk such as is encountered in gas-ether in the presence of diathermy current. If avertin cannot be used, ether may be fairly safe if a wet towel is so placed as to prevent ether fumes from reaching the field of operation.

**Post operative and convalescent care of the patient.** How long one should keep a patient absolutely quiet in bed with eyes blindfolded is a debated question. The loch bottle or pin hole glass of Lindner is indispensable to help keep the eye fixed when the bandages are removed. Another method is that of Arruga, who sews the lower lid to the eyeball with a suture through the inferior rectus. There can be no hard and fast rule since the healing process varies with each case. It is considered wise to keep the patient as quiet as possible in the hospital until the puncture points have started to become pigmented, a condition which varies from 2 to 5 weeks, sometimes longer. It can thus be seen how important is frequent postoperative ophthalmoscopic examinations.

## REFERENCES

(Those not specifically mentioned will be found cited in Krierson)

1. DODD EIDER, S. Recent Advances in Ophthalmology. P. 266, 3d ed. Philadelphia: Blackiston's Son & Co. 1934.
2. KRIERSON W. E. History of the surgical treatment of retinal separation. Arch. Ophth. 930, 397 (with extensive and up to date bibliography).
3. FISHCH, L. C. 939 graduate lecture course number 36 American Academy of Ophthalmology and Otolaryngology.
4. FISCHCH, D. and MILLER, M. Retinal detachment cured by eyeball shortening operation. Arch. Ophth. 930, 974.
5. VAIL, DORRIS. Equatorial scleral staphyloma and retinal detachment cured by excision. T. Am. Ophth. Soc. 940 (in press).
6. VAIL, P. and DORRIS, M. Operations for detachment of the retina. Traite d'ophtalmologie. Vol. 7 p. 73. Paris: Masson & Co. 1930.

# TUMORS OF THE UPPER JAW

## Particularly Tumors Related to the Sinuses

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THE upper jaw is subject to the development of practically all of the tumors that involve bony tissue and in addition may be the site of origin of cystic and calcified tumors of the odontome group. Furthermore, it may be invaded by tumors originating within the accessory nasal sinuses or by tumors of adjacent tissues within the oral cavity or nose. Malignancies of the upper jaw and sinuses have been studied and reported upon at great length so it will be my purpose to discuss more particularly the diagnosis and treatment of the common benign tumors and certain unusual tumors involving this region that are of interest to the otorhinolaryngologist.

### ODONTOMES

These tumors arise from the cells that are concerned with tooth development and may be conveniently classified as follows:<sup>1</sup>

I Epithelial odontomes Tumors in which the abnormal development takes place in the dental epithelium

1 *Dental or root cysts* These develop at the root ends of teeth that have erupted. Pulpal and root end infection, and pulp death of traumatic or chemical origin are apparently the irritative factors in their development. They may occur at the root ends of deciduous teeth. They may also develop in an epithelated granuloma left in the alveolar process at the time of extraction of an infected tooth.

A *Indeterminate type dental cysts* occur in any portion of the jaw. They are frequent in the region of the angle or ascending ramus and may be multiple. They are not attached to the root of a tooth infected or otherwise, nor will there be a history of the extraction of such a tooth. They also occur in regions where supernumerary teeth are most frequently found and may be due to supernumerary anlagen.

2 *Dentigerous or follicular cysts* In these cysts, the wall embraces not a root but the crown of a completely or partially formed unerupted and usually misplaced tooth. Some of these cysts contain cells typical of the adamantinoma.

3 *Adamantinoma or multilocular cysts* These tumors show columns or masses of epithelial cells

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<sup>1</sup>This classification is a modification of the British Dental Association classification.

of the enamel organ types—ameloblasts-cuboidal cells, and stellate reticulum. They may be found and operated upon in an early stage when they are not clinically cystic, but rather of a solid consistency. Microscopic examination, however, nearly always shows cell degeneration and beginning cyst formation of the epithelial masses. The term "epithelioma" should not be employed in the consideration of these tumors.

II *Composite odontomes* Tumors in which the abnormal development takes place primarily in the dental epithelium, and secondarily in the dental papilla, and may occur in the follicle also.

1 The abnormal development of the dental epithelium is such that the formation of numerous irregular dentine papillae results, and are calcified in one mass or sporadically.

A *Complex composite odontomes* When tooth structure is shown in the microscopic section and not in the gross specimen which appears like an irregular mass of bone.

B *Compound composite odontomes* A large number of tooth elements are present. They may be fused or be separate within a cyst cavity.

2 The abnormal development of the dental epithelium is such that the formation of two or more tooth like dentine papillae results and are calcified as one mass.

A *Germinal composite odontomes* Present fusion of teeth combined with malformation, such as masses of dentine and cementum.

B *Gestant composite odontomes* One tooth develops within another.

C *Enamel nodules or enamel pearls* The abnormal development of the dental epithelium is such that the formation of a dilated portion of the dentine papilla results and is calcified as one mass.

A *Dilated composite odontomes*  
a Fusiform type presents a widely dilated or hollowed-out foot with a normal or semiconical crown.  
b Coronary type presents dilatations and malformations of the crown portion of the tooth.  
c Radicular type presents irregular calcified masses of dentine and cementum projecting from one surface of the root.

III *Connective tissue odontomes* The abnormal development takes place in the dental tissues of mesodermic origin alone. (The dental follicle.)

1 *Cementomes* Consist of solid irregular masses of cementum (1) that may develop about the roots or crown of a tooth that eventually erupts after which the cementum may continue to enlarge or (2) may surround and destroy an unerupted



immature tooth. These masses enlarge and expand the alveolar plates.  
*Fibrous odontomas.* Apparently the same type of tumor as central fibromas (benign osteogenic tumor), and the fibromas that develop from nerve sheaths. The diagnosis of fibrous odontoma is presumed when the tumor is associated with an unerupted malformed tooth or other dental anomaly.

This classification, based on a very extended study by a committee of the British Dental Association, is to my mind most practical for the surgeon called upon to treat these conditions. Other classifications that have been proposed by pathologists tend to confuse rather than help the surgeon in the diagnosis and treatment of the individual patient. For instance, in many texts, dental root cysts (radicular cysts) are considered to be an inflammatory cyst and not a cystic tumor. While these are from the standpoint of etiology associated with root end infection, traumatic or chemical pulp death or residual alveolar process infection, their clinical course in so far as the destruction of bony tissue and the involvement of the sinuses is concerned, cannot be differentiated from that of the dentigerous cyst. Furthermore, the microscopic examination of cyst walls of both types fails to reveal any diagnostic features that differentiate the cyst wall of the dental root cyst from that of the dentigerous cyst. It is a well known fact that examinations of serial sections of the walls of dentigerous cysts show that some of them are at least potentially adamantinomas. These findings convince me that these cystic tumors should be classified in one group as epithelial odontomas and not considered separately, sometimes even in separate chapters as is the case in some textbooks. Consequently the dentigerous cysts of the maxilla present potential problems from a tumor standpoint that must be kept in mind in the consideration of the operative techniques designed to prevent the development of persistent fistulas between the mouth and the maxillary sinus or the floor of the nose by leaving in the major portion of the cyst wall.

Cystic odontomes of the dental root and dentigerous types may develop in the anterior the lateral, or posterior portions of the maxilla. As already noted, their clinical manifestations, growth, and effect upon the bony substance of the upper jaw and encroachment upon the sinuses are quite similar. The rate of enlargement of a cyst varies considerably and is difficult to determine as most patients are operated upon soon after the discovery of the presence of a cyst. Occasionally one can locate a roentgenogram taken

some years previously, showing beginning cyst formation that was either not diagnosed or was neglected. In the case of dental root cysts, one may at times estimate the duration of the cyst by the date of a severe dental traumatism, the devitalization of a tooth or the insertion of a synthetic porcelain filling. These cysts may be found at any age, although dentigerous cysts are more common during the period of the development and eruption of the permanent teeth. The direction of the extension of the cyst varies considerably. They may grow more or less equally in all directions or may extend largely in one direction. They tend to project on the labial or buccal surface of upper jaw presenting as a more or less rounded prominence. This may be soft, hard, or compressible with crepitation, depending upon the amount of loss of the overlying bone due to resorption of the alveolar plate brought about by the presence of the enlarging cyst or the presence of newly formed bone overlying the cyst wall.

These findings may also be present and demonstrable in the hard palate or the cyst may extend upward to elevate the floor of the nose to a considerable degree or may obliterate the entire maxillary sinus and even extend farther without any buccal or palatal evidences of extensive cyst formation. Cysts may expand and thin out the overlying tissues to rupture or they may be excised on suspicion of an abscess formation following which there may ensue a very low grade secondary infection. The cyst contents vary markedly in consistency and color—depending upon the types of degenerative processes affecting the epithelial and connective tissue of the cyst walls together with the character of the exudates or presence of hemorrhage modified at times by low grade infection. Very rarely an extremely acute infection may for no apparent reason involve a cyst that has been developing for months or years without producing any symptoms. Discharging sinuses and infections of a cyst in the maxillary sinus region are often confusing in the matter of correct diagnosis and treatment.

*Diagnosis.* Careful clinical examination of the oral region together with rhinoscopic examination may establish a presumptive diagnosis of the presence of a cystic odontome. If permanent teeth are missing with no history of their extraction, the presence of a dentigerous cyst should be suspected. Roentgenographic examination is essential to determine the position and extent of the tumor, the presence of unerupted teeth, etc.

Regular intra-oral dental films are useful but occlusal films of larger No. 2 size,  $2\frac{1}{2}$  by 3 inches, taken in the anterior and the oblique lateral pro-



to function normally for many years, provided the root ends are not exposed by the surgical removal of the cyst membrane. Pre-operative dental x-ray films will usually show the intimate relationship of the cyst wall to the underlying root ends and will determine the necessity of leaving the cyst wall to protect the vitality of the teeth. In more recent cases, I have left this lower portion of the cyst wall undisturbed with uniformly good results in so far as the healing of the maxillary sinus cystic cavity is concerned.

Another problem that warrants detailed discussion is that of the treatment of large cysts that not only obliterate the maxillary sinus, but also extend under the floor of the nose sometimes past the midline beneath the floor of the nose on the opposite side. If a Partsch operation is performed the postoperative course may extend over months or a year or more. If a Caldwell-Luc cyst procedure is undertaken the cystic area beneath the floor of the nose constitutes a pocket where erodates may collect, become foul smelling, and give the patient no end of annoyance and discomfort. To prevent this postoperative condition, a two stage procedure has been undertaken with gratifying results. The first procedure is a Partsch operation exposing the anterior extension of the cyst cavity but not uncovering it completely on its labial aspect. It is then treated after operation in a routine manner by gauze packing two or three times a week until the anterior extension of the cyst has filled in sufficiently to obliterate that portion of the cavity that was present beneath the floor of the nose. This may take 3 or 4 months to accomplish after which, the Caldwell-Luc cyst procedure may be undertaken and the oral incision that had remained open since the first operation is closed by undermining and suturing. The comfortable and satisfactory end-results have fully justified the time and care spent on several cases that have been treated in two stages in this manner. The prolonged period of dressings and the greater or lesser deformities that have been avoided amply repay the patient for the confidence and co-operation shown in accepting two operative procedures in order to obtain a more satisfactory ultimate result.

In case a portion of dentigerous cyst wall is left in position to prevent fistula formation or to shorten the postoperative course as already outlined, it is essential to have a microscopic examination made of that part of the cyst wall removed with the window. Any thickened or projecting portion of the cyst wall should also be excised and examined to be sure that the epithelial cells are not of the adamantinoma type. Such a condition

is found very rarely but must be kept in mind, and, if present, excision of the entire cyst wall or cauterization by diathermy should be employed.

Should permanent fistulas develop to communicate with the nose or maxillary sinus, carefully made dental restorations will largely overcome the discomfort incident to such perforations.

Atypical cystic tumors of the maxilla that involve the maxillary sinuses have come under our observation several times. They have presented combinations of cystic areas and masses of fibrous tissue and bone in association with unerupted malformed teeth. The exact diagnosis may be somewhat obscure but is likely to be a variant of a composite or fibrous odontome or an atypical osteitis fibrosa cystica—but microscopic examination will establish the benign character of the tumor tissue. The treatment is in general accordance with that already outlined for cystic odontomes depending largely upon the position and extent of the tumor.

The adamantinoma of the maxilla is very slow growing with insidious onset and consequently presents considerable difficulty in the matter of early diagnosis. Symptoms may be practically absent or there may be merely an indefinite feeling of pressure or tension. Slight neuralgic pains or tenderness referred to the maxillary sinus area may be noticed by the patient. In other cases, the symptoms are localized to the teeth and alveolar process and are likewise ill defined. This tumor may be present for many years before any definite enlargement of the maxilla may be demonstrated. Dental roentgenograms tend to be inconclusive and routine sinus films may show but slight or moderate clouding of the maxillary sinus.

These considerations account for the difficulties in diagnosis and the delay in instituting adequate treatment for this tumor. Months and years of valuable time may be lost while the patient is undergoing dental treatment or repeated punctures and irrigations of the maxillary sinus. Intranasal window operations may be performed to improve sinus drainage without the removal of tumor tissue for biopsy and thus more time may be lost. I have seen several patients whose histories suggested the presence of an adamantinoma for many years before the diagnosis was established.

I hesitate to bring into this discussion such a controversial subject as the relative merits of the intranasal antrum operations versus the canine fossa approach to the sinus used in the Caldwell-Luc procedure in the treatment of chronic maxillary sinusitis, realizing that men who employ

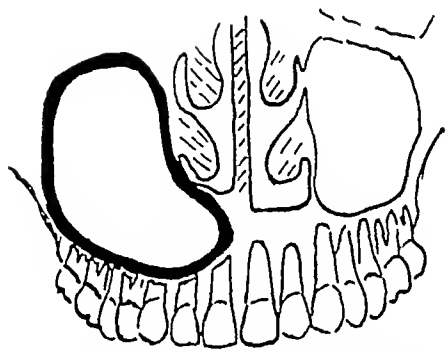
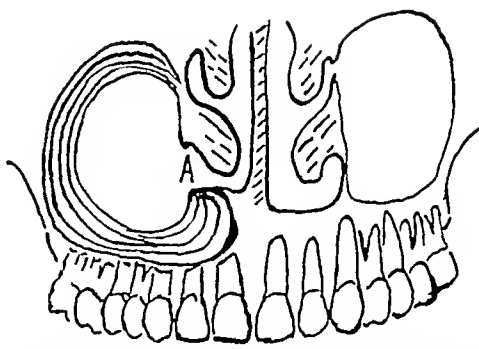


Fig 1 Two stage operative procedures for cystic tumors that obliterate the maxillary sinus and extend beneath the floor of the nose Stage I Partsch operation by means of a buccal window through which the cyst



cavity is dressed Stage II 3 to 6 months later as soon as the cavity beneath the floor of the nose has become obliterated A, Intranasal window established and surgical closure of the operative approach used in Stage I

the Caldwell-Luc procedure are greatly in the minority While I concede that in the hands of skilled rhinologists the intranasal procedures are effective and satisfactory in every particular, I do feel that the buccal approach to the maxillary sinus gives better access to, and more complete visualization of, the operative field, thus affording more thorough and accurate surgical treatment of the condition present

In my experience there have been no disadvantages associated with the Caldwell-Luc procedure other than swelling of the cheek that lasts but a few days I am sure that rhinologists who employ the Caldwell-Luc procedure will quickly develop a diagnostic sense that will differentiate between the varied appearances of chronic inflammation of the sinus mucosa on the one hand and the more serious tumors and the malignant tumors on the other hand

For this reason, I would urge that rhinologists employ the Caldwell-Luc procedure much more frequently especially in cases with obscure symptoms in order to make possible the earlier diagnosis of tumors of the sinus and to avoid the humiliation incident to prolonged sinus treatments in tumor cases

The nature of the tumor cannot be diagnosed by visual examination alone and biopsy is necessary to determine the treatment to be instituted

Adamantinomas of the maxilla and sinuses must be considered as serious tumors that may endanger the life of the patient on account of inoperable extensions or the onset of meningitis due to the extensions of the growth and secondary infection The prognosis varies with the position and extent of the tumor and the greater or lesser degree of histological activity of the tumor cells The more or less favorable position of the tumor

is a large factor in its curability, and it is obvious that the inferior anterior location affords a much more favorable prognosis than does a location extending posteriorly and superiorly This corresponds with the conclusions of Ohngren who divides tumors of the upper jaw and antrum into two groups by a plane which passes from the inner canthus in a direction backward and downward to the angles of the mandible It must be remembered that an unsatisfactorily prepared and stained frozen section may present difficulties in diagnosing adamantinomas from adenocarcinoma and at times it may be wise to postpone the destruction of the tumor by cauterization or with surgical diathermy until the day following the biopsy This will permit the preparation of a well stained permanent section making accurate diagnosis and the determination of the degree of cell activity less difficult

Adamantinomas must be completely removed and destroyed in order to prevent recurrence Surgical diathermy is the method of choice and should be employed in a thorough and painstaking manner The bony wall surrounding the tumor tissue should be cauterized thoroughly in every portion of its surfaces and any regions in which the tumor may have extended through the antral walls to the soft tissues should be carefully treated with a protected endotherm point The same meticulous care should be employed in destroying the tumor tissue that may have extended into the ethmoidal sinuses These tumors are resistant to radiation, although radium may be employed with apparent success in regions that are inaccessible to adequate treatment by diathermy Extensions of adamantinomas beneath the orbit may produce orbital displacements, exophthalmos, and a variety of inflammatory conditions of the

orbit and globe. It may be occasionally necessary to remove the eye but usually the displacement or inflammatory reaction subsides as soon as healing is complete. The postoperative course may be stormy and painful until sequestra have become separated and are removed, particularly when orbital signs and symptoms were present before the operation. Usually from 6 weeks to 3 months or more elapse before it may be determined that the margins of the necrotic bone may be pried loose and the sequestra can be removed. Healing thereafter is usually without incident and the region becomes comfortable. Examination should be made from time to time in order to be sure that all parts of the original tumor area are well healed and firmly epithelialized.

Recurrences of this tumor are due to failure to remove and destroy all tumor tissue. Such recurrences are usually of very slow growth and prognosis is still usually favorable except when situated in the posterior superior regions. It is not wise to attempt a plastic closure of the buccal opening into the operative area for 2 or 3 years, until one is satisfied that there are no evidences of recurrences—an obturator may be made or the patient may use cotton or gauze to plug the opening at meal times.

Composite (calicified) odontomes may involve the maxilla. These are sometimes associated with areas showing fibrous or cyst formations. Diagnosis is usually not difficult, as roentgenograms usually reveal the nature of the tumor. These tumors are essentially benign and do not endanger life. They do, however show a tendency to develop acute infections in the tissues adjacent to the surface of the tumor and produce a cellulitis with abscess formation. Occasionally this may occur without any previous knowledge of the presence of a calcified tumor. Several weeks should elapse following such an infection before any attempt is made to remove the tumor.

The treatment is surgical excision of the entire tumor mass and the operative approach is much the same as for the cystic odontomes. Excision of the calcified tumor may be difficult, requiring painstaking removal of overlying and adjacent bone by means of chisels or burrs in order to make possible the delivery of the tumor from its bed. The resulting defect may present quite a problem on account of an extensive exposure of the sinuses and nose together with loss of the alveolar process ridge. The operative approach is from the buccal or the incision may be made along the alveolar process ridge. If coperiosteal flaps may be retracted palatally and buccally to provide a wide exposure of the tumor area and may at the con-

clusion of the operation be sutured to close off the operative field from the mouth if conditions permit. These tumors are not likely to extend beneath the floor of the nose and the sinus tumor cavity may be made to communicate with the nose by means of a naso-antral window to thus shorten the postoperative course as outlined in the discussion of the treatment of cystic odontomes.

Fibrous odontomes or central fibromas of the maxilla can rarely be diagnosed before operation, as the x ray appearances are similar to those of the cystic odontomes. Fibromas are rare and biopsy is necessary in order to complete the diagnosis. The treatment is complete excision and the operative and postoperative treatment corresponds with that of the cystic odontomes in which the entire cyst wall is removed.

Cementomas develop slowly but may attain a considerable size to encroach upon the maxillary sinus. The x ray appearance of these tumors is similar to the composite odontomes and the operative and postoperative treatment is essentially similar in every respect.

As already noted in the introduction to this discussion the upper jaw may be the site of any of the tumors that involve bone. These may be classified according to the various modifications of the Codman registry nomenclature of the American College of Surgeons.

- I. Metastatic tumors of the jaw are rare. Metastases of carcinoma from the breast, thyroid, prostate, ovary etc. are on record. Sarcoma and hypernephroma metastasizing to the jaws has been reported.
- II Periapical fibrosarcoma is less malignant form of sarcoma that has been found lying next to the bone of the jaws. It arises in the outer layers of the periosteum or in the adjacent fascia or tendinous insertions. It does not invade the bone but may cause pressure absorption. It does not form osteoid tissue, cartilage, or bone. Metastases infrequently occur.
- III Osteogenic tumors are derived from cells concerned in the development of bone and cartilage, etc.
  - A Benign osteogenic tumors

Hyperostoses are inflammatory enlargements of diffuse type that frequently involve the malar region and tuberosity of the maxilla. Leontiasis osseus is of this type. Exostoses may occur on the lingual surface of the mandible and in the center of the hard palate, torus palatines. They have been noted to occur frequently in the tuberculous.

3. Osteomas may develop in any portion of the mandible or maxilla. When developing in the region of the condyle, the ascending ramus is lengthened, causing opening of the bite. If the upper jaw the maxillary sinus, nose, or orbit may be involved. The other facial bones may develop these tumors.

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- 4 Fibromas may occur as central tumors or in the deeper layers of the periosteum
- 5 Chondromas may develop centrally or from the alveolar margins, the palate, the coronoid, or the condylar cartilage. Pure chondromas of the jaw are rare. Tumors of this group may show combinations of cartilage, fibrous tissue and bone
- B Malignant osteogenic tumors. Osteogenic sarcomas may arise in the central portions of the jaw and in the deeper layers of the periosteum or may arise alone from the subperiosteal layer. It is often difficult to determine the exact site or origin, particularly in the maxilla where such tumors may start in the subperiosteal layer of the maxillary sinus membrane. Types
  - 1 Those destroying bone—osteolytic
  - 2 Those forming bone—sclerosing
  - 3 Those forming cartilage—chondrosarcoma
- IV Inflammatory conditions that may simulate tumors of the mandible and maxilla
  - A Osteoperiostitis (osteomyelitis) occurring in atypical forms may occasionally simulate a primary tumor of the mandible or maxilla
    - 1 Traumatic periostitis may occur in chronic form without an acute onset. Hemorrhage and resulting repair, cartilage, and bone formation may closely simulate tumor for a few months' observation will clear up the diagnosis
    - 2 Syphilitic periostitis or osteoperiostitis occurring in the second or third stages of lues may resemble a sarcoma
    - 3 Infectious osteoperiostitis—osteomyelitis
      - a. Pyogenic infection of a low grade type may produce tumefaction that necessitates observation over a period of time in order to rule out tumor formation
      - b. Tuberculous periostitis and osteitis may for a considerable time simulate tumor formation
  - B Actinomycosis of the tissues surrounding the mandible, particularly when hard, may for a time simulate sarcomas. The bony substance of the jaw is rarely if ever involved and the contour of the mandible will be seen to be normal in the roentgenogram.
  - C Osteitis fibrosa cystica occurs frequently in the mandible and maxilla. It is characterized by cystic areas without an epithelial lining, fibrosis, condensing osteitis. Other bones may also be involved. This condition may be associated with parathyroid tumors and disturbances in the calcium phosphorus balance
- V Central giant cell tumors are identical in structure to the giant cell epulides. They develop centrally and expand the jaw until the cortex is reduced to a thin shell or becomes destroyed. They are usually soft and red and present a varying number of multinucleated giant cells in a loosely woven connective tissue stroma
- VI Angiomas, benign or malignant, of the bony substance of the jaws are very rare, but have been recorded
- VII Ewing's sarcoma, endothelioma, may develop in the mandible in several areas simultaneously, destroying the bone. The tumor consists of small, polyhedral cells with no intercellular substance. Fever, pain and the x ray appearance may simulate osteoperiostitis—osteomyelitis

VIII Myelomas may involve the mandible and skull along with other bones. The myelitic substance of the bone is destroyed by the tumor cells. Albumosuria is present.

Metastatic tumors of the maxilla are rare and usually insidious in their course, presenting difficulties in diagnosis except by biopsy. The prognosis depends upon the type of tumor, its degree of malignancy and the prognosis of the primary tumor. Many of course are inoperable on this account. Metastases to the jaws of carcinoma of the breast, thyroid, prostate, and ovary have been reported as well as sarcomas and hypernephromas. A benign tumor of the thyroid metastasizing to the mandible has been reported by Ivy.

Periosteal fibrosarcoma arising on the external surface of the maxilla may necessitate the exposure of the maxillary sinus in its removal by excision. Osteogenic tumors of the maxilla may be benign or extremely malignant osteogenic sarcomas. The benign tumors are the hyperostoses, exostoses, osteomas, chondromas, and fibromas. Hyperostosis may produce a massive enlargement of the molar region and tuberosity. The buccal and palatal aspects are more particularly involved although the tumor may extend upward to encroach upon the maxillary sinus. Removal of the excess bone by chisels and curets to restore a normal contour gives satisfactory results in that production of new bone ceases. Should the maxillary sinus be exposed in the surgical procedure, it usually does not require any special treatment as the mucoperiosteal incisions may be sutured. Central osteomas, fibromas, and chondromas may also encroach upon the maxillary sinus, and their surgical removal may produce large openings into the sinus cavity. These may usually be closed by suturing. Occasionally it may be wise to make an antrobasal window through which postoperative treatment may be carried out.

Osteogenic sarcomas of the maxilla are relatively infrequent—about 10 per cent of the primary and secondary malignant tumors involving the maxillary sinus will, on microscopic examination, be found to be osteogenic sarcomas presenting wide variations of sarcomatous cellular detail which accounts for the fact that these tumors have been designated as spindle cell sarcoma, round cell, myxosarcoma, osteosarcoma, chondrosarcoma, mixed, angiosarcoma, or combinations of several types. These tumors may arise in the deeper layers of the periosteum or beneath the periosteum in the cortical or medullary portions of the alveolar process or body of the maxilla. In these cases the early symptoms may be merely

obscure dental pain or loosening of teeth, which progresses to an apparent tooth or jaw infection with suppuration and necrosis. On the other hand, the tumors may arise from the periosteum of the maxillary sinus and may grow to fill the antrum before producing definite symptoms of tumor formation. Local ulceration of the tumor within the sinus may lead to symptoms of nasal and sinus infection such as obstruction or discharge of a purulent or blood stained nature. Later nasal polyps may be seen on examination and bleeding from the nose may become frequent. The condition may be erroneously diagnosed as a chronic infection of the maxillary sinus and much valuable time is thereby lost. Continuing to grow the tumor may perforate the bony walls and extend into the cheek the orbit, the nose, or the palate.

Enlargement of the cheek of recent origin in a middle aged person is usually malignant if not of inflammatory dental origin and should not be neglected. At times, displacement of the eye may be noticed a few weeks after the onset of nasal symptoms. Early diagnosis is most essential in order to make possible adequate treatment of this extremely malignant tumor. Persistent facial pain aggravated by lying down increasing nasal obstruction of short duration, lacrmal duct obstruction, mucoid or suppurative nasal discharge particularly if blood stained, are symptoms that should be considered due to a malignant tumor until the condition has been proved to be inflammatory or benign. Roentgenograms should be made, using the standard and special projections to show the maxilla and the sinuses. Careful examinations of the films should be made to determine the presence of defects of the bony walls, which almost invariably indicate destruction by tumor formation. I have seen but one patient in which such a defect proved to be due solely to chronic inflammation.

These symptoms and examination findings should convince the surgeon that the condition is a malignant tumor and he should plan the treatment accordingly. At operation, a frozen section should be made to determine the diagnosis and the degree of malignancy.

The treatment of osteogenic sarcomas of the maxilla is destruction by diathermy supplemented by radiation therapy preferably by means of radium emanation or element from within the tumor and sinus area (5). An interval of time between the biopsy and the destruction of the tumor tends to increase the operative difficulties and should be avoided. Intratracheal nitrous oxide is the anesthetic of choice and the operative ap-

proach is either through the mouth or by means of a lateral rhinotomy depending upon the position of the tumor. Primary and secondary bleeding is controlled by packing. If persistent, the ligation of the external carotid artery may be come necessary.

This discussion of osteogenic tumors of the maxilla holds true for squamous cell epitheliomas and adenocarcinomas which are much more frequent—about 70 per cent of all primary and secondary malignant tumors of the antrum.

The postoperative course is much the same as has been described in the case of adamantinomas of the maxilla and antrum. Any defects and loss of tissue of the maxilla or cheek may be reasonably well restored by plastic surgery. This should not be undertaken for several years, until danger of tumor recurrence is apparently well past. Dental restorations of the obturator denture type may be necessary to close off the antrum or nose from the oral cavity.

As to chondrosarcoma of the maxilla, Phe-mister is of the opinion that the term osteogenic sarcoma is used too broadly at present and is of the opinion the malignant cartilaginous tumors may be recognized as a class by themselves and so designated. He reports a case of chondrosarcoma of the maxilla that terminated fatally after two recurrences with metastasis. The microscopic examination showed hyaline cartilage with extremely little calcification or ossification. This tumor filled the antrum to bulge above the gum margin. The recurrences extended through to the nasopharynx, orbit, and the nose.

Osteitis fibrosa cystica is a borderline inflammatory tumor that may involve the maxilla to produce a slowly progressing enlargement of the upper jaw. The overlying soft tissues and the periosteum are apparently not involved by the growing tumor. The molar region and the tuberosity are common sites for the development of this condition and consequently the maxillary sinus may be more or less obliterated by the gradual extension of the process in the upward direction. Symptoms are usually obscure—often limited to a feeling of pressure slight pain, or recurring neuritis. Later the patient is conscious of an enlargement of the jaw or cheek. These growths may be associated with similar lesions in the long bones and parathyroid tumor or with disturbances in the calcium phosphorus balance. Occurring in the region of the antrum these tumors are of considerable interest to the rhinologist. Some of these growths present multiple cysts readily recognized in the roentgenogram, whereas others show but massive enlargement of finely trabecu-

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ated bone similar to hyperostosis. Treatment is not standardized for this condition. Careful examination should be made to rule out parathyroid tumor. Surgical treatment is usually limited to the removal of enough tumor tissue to correct the enlargement and deformity. These growths tend to be self-limiting and regressive and the postoperative course is usually without incident. Adequate mineral and vitamin therapy is a useful adjunct to surgical treatment in the management of these tumors.

Giant cell tumors of the maxilla occur in two forms (1) the giant cell epulis, and (2) the central giant cell tumor. The epulis develops in the region of the gum margin but may extend deeply into the body of the maxilla. The central giant cell tumor tends to grow in all directions to involve the maxillary sinus and also protrude on the buccal and palatal aspects of the upper jaw. These tumors may be indolent and slow growing with relatively feeble invasive and destructive qualities or an active malicious growth which increases rapidly in size to destroy the overlying bone and extend into the adjacent soft tissues. The microscopic examination shows large numbers of giant cells in a stroma of actively growing cells of both round and spindle type. Giant cell tumors have been studied extensively with reference to their etiology, pathology, and the relationship of these tumors to solitary bone cysts and osteitis fibrosa cystica. Some authorities favor radiation therapy rather than surgical removal by curettage and cauterization. Others stress the fact that many of these tumors are not radiosensitive and when so treated valuable time is lost and subsequent surgical treatment is of necessity more radical and mutilating. Surgical treatment is the method of choice in giant cell tumors of the maxilla. Removal of the tumor tissue by enucleation and curettage of the bony cavity followed by cauterization is effective in eradicating this tumor. The operative defect will determine the nature of the postoperative treatment and the handling of the problem of sinus exposures in a similar manner to what has already been discussed.

Squamous cell epitheliomas are by far the most common primary and secondary malignant tumors of the maxillary sinus. Adenocarcinoma occurs about as frequently as the various sarcomas that may be grouped as osteogenic tumors. The

symptoms are about the same as those noted in cases of adamantinoma and osteogenic sarcoma and the treatment is essentially electrosurgical and by radiation therapy rather than by the radical surgical procedures in vogue two decades ago.

The degree of malignancy as shown in the microscopic section will determine the technique of treatment. Tumors of lesser malignancy require careful and painstaking destruction of the entire tumor by surgical diathermy and when bone is involved the periosteum is likewise treated to prevent recurrence. Great care must be taken to avoid leaving any tumor tissue in any region, and frozen sections may be made of any suspicious areas. Further destruction by diathermy may be instituted and radium seeds inserted. Highly malignant tumors should be explored and thoroughly coagulated centrally to provide adequate drainage and to produce a cavity large enough to permit the insertion of radium element and radium emanations may be implanted around the periphery of the growth. The postoperative considerations and course have already been discussed under adamantinomas and osteogenic tumors.

### BIBLIOGRAPHY

1. CODMAN, E. A. Bone Sarcoma, An Interpretation of the Nomenclature used by The Committee on the Registry of Bone Sarcoma of the Am College of Surgery 1925
2. FIGI, F. A. Malignant diseases of the mouth. J Am Dental Ass., 1939, 26 1979
3. GABELL, D. P., JAMES, W. W., PAYNE J. L. A report on odontomes. Brit. Dental Ass., 1914.
4. IVY, R. H. Thyroid tumor of the mandible. Ann Surg., 1931, 94 437
5. NEW, G. B. Malignant diseases of the paranasal sinuses. Am J Surg., 1938, 42 170-173
6. ÖHRNGREN, L. G. Malignant tumors of the maxillo-ethmoidal Region. Acta oto laryngol., 1933, Supp 19
7. PARTSCH, C. Deutsche Monatschr f Zahnhe, Berl., 1910, 28 252-260
8. PHEMISTER, D. B. Chondrosarcoma of bone. Surg., Gynec & Obst., 1930, 50 216-233
9. WALDRON, C. W. Chapter entitled "Tumors of the oral cavity—oral pathology" in Bunting's Oral Pathology Philadelphia Lea and Febiger, 1929
10. Idem. Follicular odontomata of the superior maxilla. Surg., Gynec & Obst., 1916, 23 473
11. WATERS, C. A., and WALDRON, C. W. Roentgenology of the accessory nasal sinuses describing a modification of the occipitofrontal position. Am J Roentgenol., 1915, 2 633



# NEUROSURGICAL ASPECTS OF FACIAL INJURY

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**G**ROSS injury of the nerve supply of the face is comparatively rare in trauma of this region. This is the more surprising when we recall the rich and complicated nerve supply of the head. Nearly all of the twelve cranial nerves are distributed in this region, including the nerves of special sense—smell, sight, taste, and hearing. Tactile sensibility is transmitted through the fifth cranial nerve by three great branches leaving the base of the skull through three separate foramina of exit. The facial muscles are innervated by the seventh cranial nerve that leaves the cranial cavity through a tortuous bony canal in the petrous portion of the temporal bone.

That this rich nerve supply should escape injury is explained by certain embryological and anatomical factors. The base of the skull, it will be remembered, is embedded in cartilage, and becomes ossified comparatively early in life. The base of the skull becomes a massive block of cancellous bone whose otherwise cumbersome weight and size are relieved by numerous cavities lined by mucous membrane and connected with the nose, the paranasal sinuses.

Trauma severe enough to fracture this basilar block of bone produces only fissures unless it is of such severity that the skull is crushed when death immediately ensues. Though fissure fracture of the base of the skull may cause grave consequences from resulting intracranial hemorrhage, it is only when the fracturing fissure passes through, or in the neighborhood of, one of the many foramina of exit of the cranial nerves that injury to these structures takes place.

As there is little or no displacement of bone fragments in fractures of the base of the skull, the fractures themselves are disregarded and our attention is centered on the complications—hemorrhage, edema, or nerve injury.

The characteristic reparative process of the bones of the skull is of great surgical importance. The massive temporary callus following fractures elsewhere in the body is not seen. Permanent repair of fracture of the skull is also accompanied by a minimum of permanent callus. Thus no bony masses mark the site of repair and the line of fracture returns almost to its normal configuration.

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This fortuitous phenomenon prevents these fractures from either encroaching on the cavity of the skull proper or on the foramina of exit of the cranial nerves. If compression of a nerve occurs from hemorrhage immediately following injury we may expect the compression to subside promptly with absorption of the clot. We also expect no permanent interference in the function of the nerve from resulting callus formation or exostosis.

Therefore, the dysfunction of the cranial nerves following trauma of the head is usually transient paralysis. Unless the particular nerve is actually severed or crushed by the injury its function returns in a comparatively short time.

Certain nerves seem to be more easily hurt than others. This is probably best explained by the narrowness of their foramina of exit, which permits minimal displacement or hemorrhage to disturb the delicate axon cylinders without gross injury of the nerve trunks themselves. The sixth cranial nerve supplying the external rectus muscle of the eyes is the most commonly hurt. Hence a transient extra-ocular palsy with diplopia is not uncommon in cases of fracture of the base of the skull. Injury of the other cranial nerves supplying the eyeball and its extra-ocular musculature is much more rare.

In third nerve injury the greatest permanent disability is ptosis of the eyelid because of the deformity produced. Anchoring the lagging eyelid to the frontalis muscle by a fascial band is the best treatment for this defect. The eyelid is elevated to a more normal position and can be raised by contraction of the ipsilateral frontalis muscle.

The next most commonly affected cranial nerve to be injured in fracture of the base of the skull is the seventh, or facial, nerve. Since it supplies all of the muscles of the face, its injury produces marked disfigurement and disability.

A total paralysis of the facial nerve produces complete relaxation of the corresponding side of the face. The patient is unable to close the eye, with resulting danger to that organ. Because the mouth cannot be closed on the affected side, there is constant dribbling of saliva and marked interference with mastication. Even a partial facial palsy is disfiguring. As expressional movements are principally affected, the sufferer feels the embarrassment acutely and begs for relief.



Fig 1

Fig 2

Fig 3

Fig 4.

Fig 1 Case 2 Complete dehiscence of the left seventh nerve repaired by 15 millimeter graft from the anterior cutaneous femoral nerve Before operation Face in repose

Fig 2 Case 2 Before operation Patient smiling

Fig 3 Case 2 After operation Face in repose

Fig 4 Case 2 After operation Patient smiling and closing the eye

Fortunately, surgery has something to offer these patients. The deformity of the face may be improved by the insertion of fascial bands in the subcutaneous tissues. These are attached to the angle of the mouth, the nasolabial fold, and to the upper and lower eyelids, and are anchored in the temporal fascia. Such an operation restores the facial symmetry and prevents overstretching of the affected muscles. It is a great relief to these unfortunates, but, of course, does not restore the function to the paralyzed muscles.

Re-innervation of the affected musculature may be accomplished by direct repair of the divided nerve, or by anastomosing a neighboring motor nerve with the distal portion of the paralyzed nerve. The latter operation has enjoyed a good deal of popularity since it was first done by Sir Charles Ballance in 1895.

He divided the spinal accessory nerve in the apex of the posterior triangle of the neck and anastomosed its proximal segment to the distal segment of the freshly divided facial nerve. Later Ballance suggested the use of the hypoglossal nerve. This operation, I believe, is now the more popular procedure since the accompanying movements of the tongue are less disfiguring and disabling than the movements of the shoulder that accompany spinal accessory facial anastomosis.

The results of these procedures, as satisfactory as they sometimes are, do not compare with the results accomplished by direct nerve suture or even to nerve graft of the seventh nerve itself.

Ballance and Duel carried out exhaustive researches on monkeys and showed that grafting

the facial nerve in the fallopian canal is usually more successful than grafting of other peripheral nerves.

Unfortunately, too many facial palsies are seen following mastoid operations in which not only may the nerve be severed but there may be actual destruction of a portion of the nerve so that direct suture is impossible. In these cases the insertion of a graft from a superficial cutaneous nerve has brought about results just as satisfactory as the nerve anastomoses and without the accompanying movements of the shoulder or tongue.

Permanent injury to the fifth cranial nerve is seldom seen in facial trauma. When it does occur the only result is anesthesia of the area of distribution of the affected branch, or perhaps paralysis of the muscles of mastication on one side. This leads to little or no difficulty and surgical repair is not indicated.

It is thus seen that practically the only neurological complications of injuries about the face are a transient ophthalmoplegia, anesthesia of the face, or facial paralysis. In rare cases in which permanent nerve injury occurs the only one demanding treatment is paralysis of the seventh or facial nerve.

The operation of choice for facial paralysis is direct suture of the divided nerve. If this is impossible, nerve grafting should be resorted to, and as a last resort, if the previous operations cannot be accomplished, or if the results are not satisfactory, anastomosis of a neighboring motor nerve to the distal portion of the paralyzed nerve may be done.

I have had the opportunity to take part in the treatment of facial paralysis following mastoidectomy. An otolaryngological confrere, Dr William H. Jenkins, of Washington, D. C. and I have operated on several of these patients with very satisfactory results. The injuries, of course all occurred to that portion of the nerve in the fallopian canal. They ranged from incomplete division to total division, or to dehiscence of as much as 30 millimeters.

Direct suture was possible in 1 case. Grafting of a portion of the external cutaneous nerve of the thigh, or of the sural nerve from the calf of the

leg had to be done in 3 cases. They all show beginning return of motion in about 5 months. Excellent results occurred in an average of 3 months. In no case was there failure to obtain voluntary motion and complete restoration of the facial symmetry.

#### REFERENCES

- BALLANCE, SIR CHARLES, and DYER, ARTHUR. B. T. Operative treatment of facial palsy. *Arch. Otol.* 1917, 5, 70.  
BLAIR, VILRAY P. Surgery and Diseases of the Ear, Nose and Throat. 2d ed. St. Louis, Mo.: C. V. Mosby Co. 1917.

## BODY SECTION ROENTGENOGRAPHY AS A DIAGNOSTIC AID TO THE OTOLARYNGOLOGIST

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MANY surgeons are familiar with some form of body section roentgenography and what it can accomplish, but, for the benefit of those who have had no contact with this method, a brief review of its history and the principles involved is in order.

The ordinary roentgenogram is really a composite of all the structures lying in the path of the x-ray beam, because all structures capable of absorbing the ray cast their shadows. Unwanted shadows cannot be separated in ordinary roentgenography except by varying the tube-object relationship and by making stereoscopic films. These leave much to be desired. The superfluous images greatly limit the usefulness of roentgenography and their elimination has always been one of the chief problems of the radiologist.

Bocage (3) of Paris was the first worker to attack this problem successfully. He found that unwanted shadows could be dispersed to a remarkable degree by imparting co-ordinated, synchronized movement of x-ray tube and film about a fixed point during the exposure. All objects in the plane about which movement took place would be so to speak, "in focus and clearly defined on the roentgenogram and those outside

of the plane, out of focus and blurred on the roentgenogram. Bocage devised an apparatus carrying out this principle and applied for patent in 1921. He did not construct his machine which he called the *botome* until 1938 (4) and in the meantime several other investigators working independently had discovered this principle and devised other types of apparatus. Between 1912 and 1938 there appeared the *stratigraph* Vallebona, the *planigraph* of Zieders des Plantes, the *tomograph* of Grossmann and Choulot, the *laminagraph* of Kieffer and several modifications of these. Each worker coined a term for the type of roentgenography done with his apparatus, and as a result, the literature contains discussions of "stratigraphy," "planigraphy," "tomography" and "laminagraphy" all more or less synonymous and used indiscriminately. To avoid the confusion which naturally results from such multiplicity of names, we have strongly urged the "stratigraph," "planigraph," etc., be restricted to work done with the apparatus from which each word is derived, and that a generic term be used to cover work done with all these types of apparatus, and have used "body section roentgenography" consistently for this purpose. Among the words suggested by others is Bocage's "radiotomie," which if Anglicized and popularized would be most satisfactory because of its etymological correctness. A more elaborate discussion of the chronological development of body section

From the Edward Mallinckrodt Institute of Radiology and the Department of Otolaryngology, Washington University School of Medicine.  
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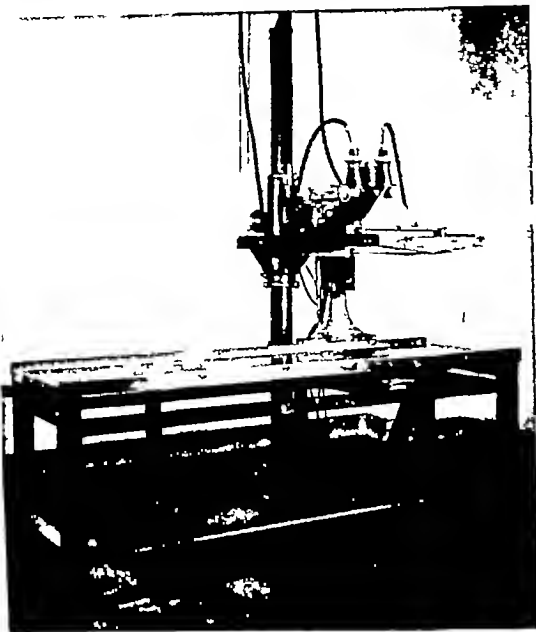


Fig 1 Photograph of the laminagraph.

roentgenography will be found in the publications of Andrews

In all body section roentgenography, regardless of the method and apparatus employed, there is the same objective in view. This is to disperse overlying and underlying shadows and leave a selected layer in the body relatively unobscured. Another objective is to visualize as thin a layer as possible because minimal contrast in density in such a layer can be brought out. This is called the "depth of focus" of the apparatus. As a general rule, the more compound the movement of tube and film during exposure, the more efficient the dispersion of unwanted shadows. These two points comprise the fundamental value of body section roentgenography in normal anatomical structures. When pathological states produce abnormal increase of density or the converse, or induce unwanted shadows, body section roentgenography is of the utmost value.

The clinical work which will be presented was done with the laminagraph, which was invented by Mr. Jean Kieffer, of Norwich, Connecticut (Fig 1). This apparatus differs from all other types and combines all the mechanically possible co-ordinate movements of tube and film, as far as known, and these can be varied as desired. The spiral movement has proved the most satisfactory, and in routine clinical work we have used it almost exclusively. With this movement the laminagraph

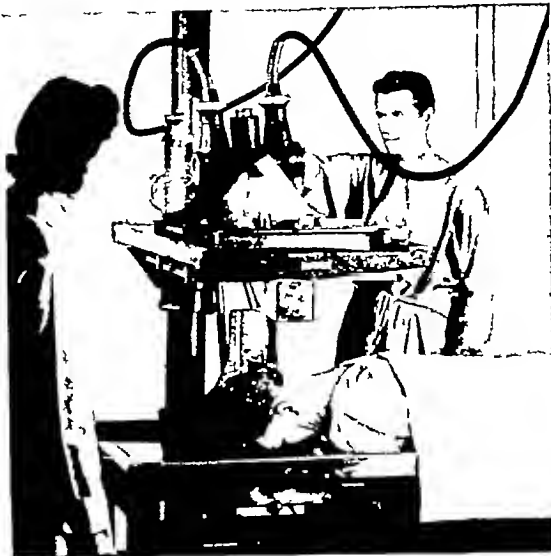


Fig 2 Position of patient for laminagraphic examination of the paranasal sinuses. Films made at 4, 5, and 6 centimeters from the table top usually suffice.

has demonstrated superiority in the symmetry of its dispersion of unwanted shadows, or blurring. Like the tomograph and its simpler modifications, our apparatus can be used only with the patient in the recumbent position, whereas the com-

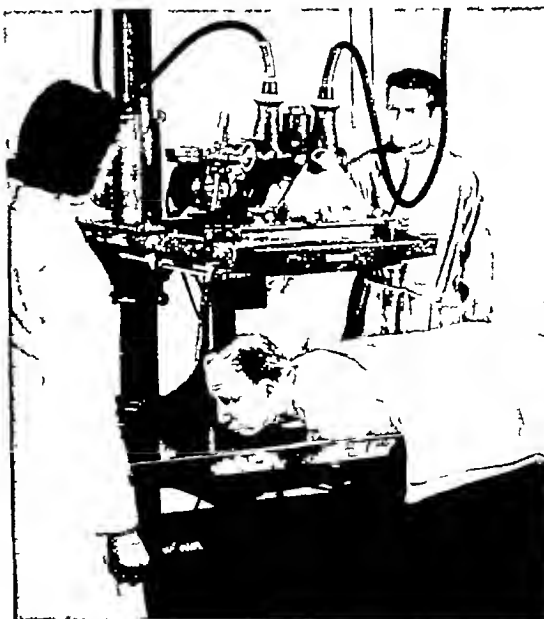


Fig 3 Position of patient in making laminagraphic examination of the larynx.



Fig. 4. Case A. S. The kymograph shows extreme supra-orbital extension of an ethmoidal cell. The possibility of this extension has been stressed by Mosher in reference to failures of frontal sinus operations in which the presence of such cell is not known. Left, conventional film. Right, kymograph (4 centimeters).



Fig. 4b

mercial planigraph, the biotome and the stratigraph utilize the erect position.

In considering the clinical applications of this method, one must constantly keep in mind its

primary objective, the dispersion of overlying and underlying shadows. It follows that in those regions where there is a maximum of these shadows the method will be of the greatest value.



Fig. 5a



Fig. 5b

(Legend on opposite page)



Fig 5c



Fig 5d



Fig 5e



Fig 5f

Fig 5 Case 2, R. L. Supra-orbital extension of frontal ethmoidal cells, marked septal deformity and changes in density in ethmoid and sphenoid sinuses. Second series of films of same patient shows corrected septal deformity with

considerable clearing in ethmoid sinuses. There is still some blurring in left sphenoid sinus. a, b, c, Pre-operative laminagrams taken at 2, 5, and 6 centimeters. d, e, f, Post-operative laminagrams at same depths.



Fig. 6a

Fig. 6. Case 3, H. A. The laminographic series illustrates wide variations of the ethmoid cells, supra-orbital extension of anterior ethmoiditis and marked extension or invasion of the maxillary sinuses. a, Conventional film, and b, c, d, e, f, laminagrams at 3, 4, 5, 6, and 7 centimeters.



Fig. 6b

Unwanted shadows produced by a pathological process have, in our experience, been most frequent in the respiratory tract. In certain of its portions there are a number of normal structures, the shadows of which it is desirable to eliminate, for example the bones overlying the paranasal sinuses, the ribs and sternum in the chest, and the spine in the region of the larynx. It is in this field that body section roentgenography has its forte and its usefulness has been repeatedly demonstrated by many workers.

In the examination of the chest, of which we have made 40 laminagrams, we have found cavities and consolidation in the lungs which were not apparent either roentgenoscopically or in conventional films. The method has been of little value in early cavitic disease in the lungs. However excavation has been shown where there was minimal change. It is undoubtedly true that the absence of grosser changes, such as cavity and consolidation, can be established with the same degree of accuracy as their presence.

The location, size and physical characteristics of pulmonary cavities can be accurately determined. Therefore, the surgeon, knowing in advance the exact location and nature of the lesion, can plan his approach with assurance.

The laminagraph can clearly reveal the tracheobronchial tree and has revealed bronchial branches as small as 3 to 4 millimeters in diameter. Dis-

location, impingement or distortion, and termination through obstruction have been clearly shown. In cases in which carcinomatous infiltration has been diffuse absence of bronchial branches has been shown, and dislocation of branches in the adjacent, healthy lung has also been revealed. Of course, this applies only to those early cases in which suppuration and abscess formation have not occurred.

In the examination of the paranasal sinuses the problem of superimposed structures has always been troublesome, and 3 years ago we predicted that "laminagrams should aid materially in such conditions as petrositis of the temporal bone conditions involving the temporomandibular joint and deep-seated paranasal sinuses, to mention only a few anatomical regions. At present, so accurate is the laminagraphic diagnosis of paranasal sinus disease that requests for these films by the otolaryngological surgeons are sent in almost daily (Fig. 2).

The second basic principle of body section roentgenography, namely the thinness of the layer roentgenographed, is important in the examination of the paranasal sinuses because it has bearing on the minimal contrast in density. In the examination of the ethmoid cells laminagrams reveal the size, position, extensions, and other anomalies, and the pathological states far beyond anything possible with standard x-ray procedures,



Fig 6c



Fig 6d



Fig 6e

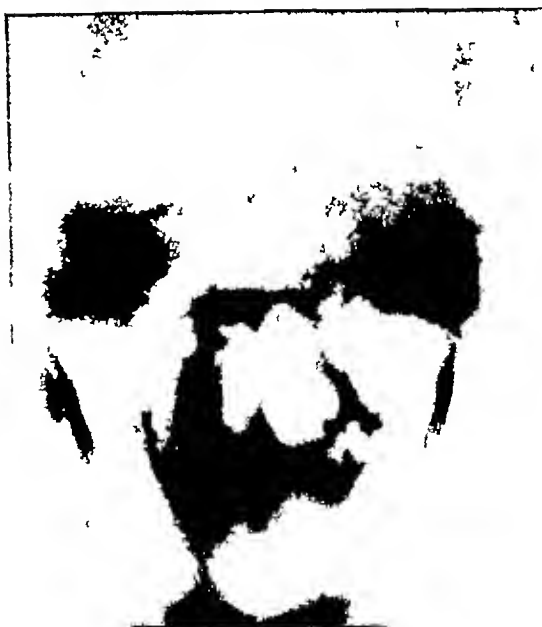


Fig 6f

(Legend on opposite page)

however extensively they may be carried out. This is also true of the sphenoid group both in the anteroposterior and lateral projections. The conventional films of the maxillary sinuses generally

suffice, but there is the occasional case in which a pathological condition is revealed with lamina-grams when it was entirely unsuspected even when contrast media were employed





Fig. 6a

Fig. 6. Case 3, H. V. The laminographic series films traces wide variations of the ethmoid cells, supra-orbital extension of anterior ethmoid and partial extension or invasion of the maxillary sinuses. a, Conventional film, and b, c, d, e, f, laminograms at 3, 4, 5, 6, and 7 centimeters.



Fig. 6b

Unwanted shadows produced by pathological process have, in our experience been most frequent in the respiratory tract. In certain of its portions there are a number of normal structures, the shadows of which it is desirable to eliminate, for example the bones overlying the paranasal sinuses, the ribs and sternum in the chest, and the spine in the region of the larynx. It is in this field that body section roentgenography has its forte and its usefulness has been repeatedly demonstrated by many workers.

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this method when it is impossible to do so with conventional films because this joint is heavily overlaid by the zygomatic process and other bony structures. Deformities, erosion, and fractures of the condyle and glenoid fossa have many times been revealed, and the laminagraph has proved of great value in the diagnosis and treatment of the "temporomandibular syndrome." This has been reported by Bleiker and by Pippin and associates.

The larynx can be investigated to great advantage by this method as has been demonstrated by Canyut and Gunsett, in France, Leborgne, of Montevideo, and Howes and Caulk, in this country (Fig 3). Mobility of the vocal cords can be investigated in different phases of phonation, and deviation of the air columns in the larynx, encroachment on the air passages by new-growth and edema, and increase in its size through ulcerating processes can be clearly shown. This is of particular value in the subglottic region, inaccessible to the laryngoscope. The exact clinical value in the diagnosis of subglottic regions has not yet been established. Leborgne considers this method of great value but properly states that it should be supplemented by direct laryngoscopy and also the lateral standard view of the larynx. We cannot agree to the importance of the latter. In our experience certainly the lateral laminagrams of the larynx have been valueless probably because that structure is too great a distance from the film for this type of examination.

By varying our factors during  $3\frac{1}{2}$  years of experience we have worked out a technique for the laminagraphic examination of the paranasal sinuses which has become approximately standard in our clinic. This has been described elsewhere. In general it may be said that standard roentgenography should always precede the laminagraphic examination so that the films may be used as a guide. When the laminagrams are made, the patient is placed in the prone position with the plane of the face parallel to the top of the table. In the routine method, films are made at 4, 5, and 6 centimeters from the plane of the face. This covers the anterior and posterior ethmoid cells and the sphenoids. These planes were established by experimental work with cadaver heads and are, for all practical purposes, accurate. As has been previously stated, the standard film usually suffices in the examination of the maxillary antra, but occasionally laminagrams are needed, not only for the maxillary antra, but also for the frontal sinuses. In that event additional laminagrams are made. For the frontal sinuses these are 0.5 and 1 centimeter, and, if the frontal sinuses have a great anteroposterior dimension,  $1\frac{1}{2}$  to 2 centi-

meters in addition. To cover the maxillary antra laminagrams at 2 and 3 centimeters in addition to the routine 4 centimeter film are sufficient.

Sluder stated, "The x-ray, in my experience, has failed to help in the diagnosis of hyperplastic post-ethmoidal and sphenoidal disease. It is of paramount value in determining cell anomalies, showing probes in positions which determine these."

Cone, Moore, and Dean reported on the relationship of paranasal sinus disease to ocular disorders as studied by laminagraphy. Changes in density of the posterior sinuses and variations in development were demonstrated. Pathological studies of tissue removed and the clinical improvement after treatment suggest that sinus disease is an important cause of ocular involvement.

S. Salinger has informed us regarding a patient with optic neuritis in whom disease of the posterior sinuses was discovered by laminagraphy. Conventional roentgenography was inconclusive. Recovery followed surgical drainage of the sinuses. Weve and Ziedes des Plantes reported a case of optic atrophy and paresis of the extra-ocular muscles due to an isolated lesion in the ethmoid bone which was not seen in the routine roentgen films but which showed up beautifully in the planigraphic studies at a depth of 5 centimeters.

Sluder, in 1927, stated,

"The frequency of headache without recognizable systemic or organic neurological basis is well known. The mystery of the etiology of many eye lesions is well known. From a very extensive experience with such cases I am led to the belief that their explanation is to be found in the hyperplastic lesion of the post-ethmoidal-sphenoidal district, to a degree of frequency that, could it be put into percentages, would astonish us all, however familiar we may be with such cases. At the same time it must be clearly understood that I do not at all believe that lesion to be the explanation of all such cases."

Today the relationship of sinus disease to ocular disturbance remains controversial. The frequency of optic-nerve involvement in patients with multiple sclerosis is well known. It has been suggested that not only the optic-nerve involvement but also the lesions of multiple sclerosis may be caused by invasion of the nervous system by way of the sinuses. Stark stated, "one (multiple sclerosis) being an advanced stage of the other (retro-bulbar neuritis)."

The improved methods of study of virus diseases and their possible extension by way of the respiratory mucous membrane has been reviewed in the Harvard Symposium (17). It is possible that numerous controversial questions may be answered when more exacting studies are made.

The value of laminagraphy is best demonstrated by the unquestionable information which its use



Fig. 7. Case 4, J. W. These two laminograms illustrate marked differences in densities in the ethmoid and maxillary sinuses. The film above is pre-operative, that below postoperative. Both were made at 5 centimeter depth. The patient was a child with an orbital involvement secondary to sinus disease.



Fig. 8. Case 5, L. B. This laminogram at 4 centimeters above shows bilateral involvement of the ethmoid sinuses in patient suffering from bilateral retrobulbar neuritis. The history in this case was previously reported and is included here only because it is our firm belief that laminography will prove to be of the greatest value in patients with posterior sinus disease and serious eye disorders in whom all other methods of examination may be unsatisfactory.

So far we have made no practical application of this method for studying the pneumatic structure of the temporal bone. However the auditory canals can be revealed throughout their extent in those rare cases of non-development of the auricle. This is the most accurate way of establishing enlargement of the internal auditory meatus in suspected eighth nerve tumors. We have had operative confirmation of laminographic findings in 3 cases. Any alteration of the auditory canal, either enlargement through soft tissue growth or decrease in size through bony growth, is discoverable with this method. The presence and the size or the absence of the groove for the lateral sinus can be shown in adults. However it is improbable that this would be possible in younger patients because of slight development of the groove, and unfortunately it is in such cases that this knowledge would be of the most value. There is evidence to suggest that a thrombosis of the lateral sinus can be visualized with laminograms.

The condition of the articulation of the mandible with the temporal bone can be established by

this method when it is impossible to do so with conventional films because this joint is heavily overlaid by the zygomatic process and other bony structures. Deformities, erosion, and fractures of the condyle and glenoid fossa have many times been revealed, and the laminagraph has proved of great value in the diagnosis and treatment of the "temporomandibular syndrome." This has been reported by Bleiker and by Pippin and associates.

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The value of laminagraphy is best demonstrated by the unquestionable information which its use

permits in showing variations in cell development. Interpretation of varying densities of individual cells may remain controversial. The possibilities are shown in the cases which illustrate this text.

In evaluating body section roentgenography it is well to remember that this method must be judged as an adjunct to conventional roentgenography and not as a substitute for it. As such it is an invaluable aid to the otolaryngologist, for laminagrams reveal changes in the sinuses undetectable by other methods and should be used *if a sincere effort in establishing the diagnosis is to be made.*

# BIBLIOGRAPHY

- ANDREWS, R. J. Planigraphy I, introduction and history. *Am. J. Roentgenol.* 93, 30 573-587.
1. BLANKIN, R. Ear disturbance of temporomandibular origin. *J. Am. Dental Ass.* 91, 5 390-399.
2. BRACK, A. E. M. French patent No. 514,454.
3. Idem. Apparatus for roentgenography of anatomic layers with bistome. *Bull. et ann. Soc. electro-radiol. med. France*, 91, 30 6-6.
4. CAVOTT, G., and GOSSETT, A. La tomographie ou planigraphie du larynx pathologique. *methode des coupes ou sections radiographiques*. *Ann. d'oto-laryngol.*, 91, 7 pp 987-994.
5. CATLER, R. M. Personal communication.
6. CONY, A. J., DEAS, L. W., and MOORE, S. Relationship of paranasal sinus disease to ocular disorders: new critical method of its diagnosis by laminographs. *Laryngoscope*, 93, 49 374-391.
7. GEORGEWICK, G. Tomography I and II. *Fortschr. u. d. Geb. d. Roentgenstrahlen* 93, 5 6-80 and 9-300.
8. HOWES, R. E. Sectional radiography of the larynx. *Radiology* 93, 33 586-597.
9. KERRICK, J. The laminograph and its variations: the applications and the implications of the planographic principles. *Am. J. Roentgenol.* 93, 30 497-515.
10. LINDENBERG, F. E. Tomography and cancer of the larynx. *Arch. Otol.*, 91, 3 4 9-415.
11. PERRY, R. N., MOORE, T. R., McCULLOCK, A. J., and MOORE, S. A method of repositioning the mandible in the treatment of lesions of the temporomandibular joint. *Washington University Dental Journal*, 44, 6 97-100.
12. SALZBERG, S. Personal communication.
13. SIEGEL, GREENFELD. *Nasal Neurology: Headache and Eye Disorders*. St. Louis, C. V. Mosby Co. 917.
14. STARR, H. H. Retrobulbar neuritis, secondary to disease of the nasal sinuses. *J. Am. M. Ass.* 92 77 678-681.
15. VALLEJONCA, A. Modified technique of roentgenographic dissociation of shadows applied to the study of the skull. *Radiol. med.* 93, 7 1090-1097. *Abstracted Radiology*, 93 7 647.
16. VINTAS and RICHMOND DISEASES. Cambridge, Massachusetts, Harvard University Press, 912.
17. WITTE, H., and ZIMMERER DES PLANTER, B. G. Morphographischer Nachweis einer Nebenschilddrüsenerkrankung mit orbitalem Komplexion. *Ophthalmologica*, 93, 97 346 (S. Salinger's translation).
18. ZIMMERER DES PLANTER, B. G. A new method of differentiation in roentgenography (planigraphy). *Acta Radiol.* 93, 3 82-9.

## TRENDS IN CATARACT SURGERY

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THE vast amount of literature appearing within the past decade is definite evidence that interest in cataract surgery is not waning. It is also proof that steady progress is being made, for while not every article is a real contribution it does show thought and out of so much thought must come some good. For example the presentation of so many variations in cataract sutures, although confusing, has made us realize the desirability of accurate wound closure. Similarly the oft-repeated debate of extracapsular versus intracapsular extraction has led to the realization that each has its place.

*Preliminary examination* During this decade our attention has been directed repeatedly to the necessity for careful pre-operative physical study of every patient, although little that is new has appeared. While reporting on postoperative complications Berens and Bogart have pointed out the prophylactic value of such an examination. The pre-operative administration of vitamin C has been advocated by Urbanek and Albrecht on the theory that old patients with cataracts frequently have vitamin deficiencies. More care is taken to control the diabetic and arteriosclerotic patient before operation but in general no great advances have been made.

A necessary part of the complete ocular examination should include a measurement of the intra-ocular tension. This point, which was emphasized for many years by the late John M. Wheeler as a safeguard against the coexistence of glaucoma and cataract, has recently been adopted as a routine measure.

The value of conjunctival smears and cultures as a pre-operative prophylactic measure is still debated. There are some, e.g., Gailey, Herrenschwand, and others, who are of the opinion that they are useless, while others, Elschmig, Kapuscinski, and others, will not operate in the presence of a positive smear—gram positive diplococci—without culturing the organism on bouillon and blood agar plates to determine its pathogenicity. Pre-operative treatment of the conjunctiva is also not standardized. Elschmig and Goar use oxy-cyanide of mercury 1:5000 and Wright (55) 10 percent argyrol for one week before operation while others

use 0.5—1 per cent silver nitrate or argyrol 25 per cent one hour before operation and still others use nothing but thorough lavage on the operating table. The advisability of pre-operative sedatives seems generally accepted. Those most favored at the present time are nembutal and sodium amytol.

*Anesthesia* In addition to the usual instillation of a local anesthetic some form of akinesia is widely used. In 1914 Van Lint described his method of producing a temporary paralysis of the branches of the facial nerve by infiltration anesthesia along the outer orbital margin. After several modifications this was followed by Wright's (56) suggestion in 1923 that the nerve be blocked at its point of emergence from the stylomastoid foramen. O'Brien, in 1929, described his technique for blocking the facial nerve at a point just external to the condyle of the inferior maxilla. The necessity for some form of akinesia is so universally recognized today that it is difficult for us to realize the newness of this safeguard.

The retrobulbar injection is not new, for one finds that Hermann Knapp, in 1884, used it successfully in a case requiring an enucleation. However, its widespread use in cataract surgery is of comparatively recent date. Enthusiastic approval of retrobulbar anesthesia is shared by many but few go as far as McCool and Dickey in believing that "if we were obliged to discard all the measures which we use to safeguard the eye, save one, we would unhesitatingly retain retrobulbar injection." The fear of an orbital hemorrhage has caused some operators to use instead an injection into Tenon's capsule, for example, Stallard. Still others, Hartshorne, for example, point out that satisfactory anesthesia can be accomplished by local instillations and subconjunctival injections. Although orbital hemorrhages do follow retrobulbar injections it is rare, as was strikingly shown by Atkinson. He collected data on 8,000 retrobulbar injections and found only 8 orbital hemorrhages, 5 of which were admittedly due to faulty technique. He correctly urges the use of a 3.5 centimeter needle as a safeguard against vessel injury at the apex of the orbit. Arruga believes that the use of a sharp needle is contra-indicated while Elschmig stresses the importance of quick, energetic compression immediately after the injection. Gailey, Kubik, and others think that a slow injection of novocain ahead of the tip of the

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needle reduces the frequency of an orbital hemorrhage. The reduction in intra-ocular tension which follows the injection is the strongest argument for its use in intracapsular extraction and is a definite hindrance to its use in extracapsular extraction. Those operators using the extracapsular extraction exclusively rarely employ it, while those using both methods use it only when the intracapsular extraction is contemplated.

Davis (10) Laval, Spaeth (48) and others have reported the successful use of avertin anesthesia in cataract extraction in unco-operative patients. Graves has advocated paraldehyde anesthesia per rectum supplemented by omnopon. The newer intravenous anesthetics have also been used—Froeschetti, Gil, and Stallard—but the vast majority of surgeons still use a local anesthetic.

**Retraction suture.** The forceps fixation of the superior rectus as described by Angelucci has been supplanted by the use of a retraction suture under this muscle. This method of controlling the movement of the eyeball has gained in popularity until today it is looked upon by many as one of the necessary safeguards in cataract extraction. Most operators pass a suture through the conjunctiva and the stump of the superior rectus. Graves, however, believes that the conjunctiva should be dissected up and the suture introduced into the tendon alone. Bartels and Wright (56) think that the use of the suture predisposes to prolapse of the vitreous because if too much traction is made upon it in an endeavor to direct the gaze downward a dangerous bulging of the wound occurs. Beach and McAdams, Lowenstein, Saint Martin, Vogt, and others urge skiness of the superior rectus instead of the suture as the safest method to prevent an upward rolling of the eye. It can be said that some form of control over the upward movement of the globe is very desirable in unco-operative cases. It is true the suture has certain disadvantages but skiness producing a complete inability to rotate the eye upward predisposes to wound gaping and vitreous loss. It seems logical therefore to introduce the suture and employ it whenever needed. It should be gently held and if the patient does not co-operate satisfactorily not unduly drawn on particularly after delivery of the lens as this may cause vitreous prolapse (Buxton). The use of skiness has diminished the frequency of the need of canthotomy but it is advocated in prominent eyes or whenever the lids exert even the slightest pressure upon the globe in the region of the external canthus.

**Incision.** The corneal incision is used by a few operators who believe that a conjunctival flap is too bloody (Appelman, Jackson) but the vast

majority of surgeons prefer some form of conjunctival flap. Various techniques have been described some prepare the flap before starting the incision while others make it with the cataract knife and leave a conjunctival bridge. Wright (56) O'Connor McReynolds, and others advocate the conjunctival bridge in complicated cataracts. It was suggested as a safeguard prior to the use of sutures and while still employed is less widely used now that the value of accurate wound closure is so generally accepted.

Most surgeons still prefer the Graefe cataract knife for making the incision although a few advocate a keratome incision enlarged with scissors. This method has never gained in popularity. In this connection one notices that many cataract sections are made small to insure proper location and to avoid injury to the iris and then subsequently enlarged with scissors—a justifiable procedure whenever one is operating in the presence of a shallow anterior chamber but not with one of normal depth. A section made with scissors is rarely as smooth as one made with a knife. Scattered throughout the literature one finds the recommendation that in the event of the iris coming in front of the knife during the incision the operator should proceed with the incision, even cutting the iris if necessary. Under these circumstances the operator in his endeavor to avoid the iris makes an incision well anterior in the cornea or if the iris is cut has but little control over the shape, size and position of the coloboma. This teaching was strenuously opposed by the late John M. Wheeler, who believed that the knife should be withdrawn immediately and the section completed with the scissors.

**Sutures.** As long ago as 1869 Williams advocated suturing the cataract incision, pointing out that by securing a more immediate union, we not only avoid ulceration of the border of the flap and prolapse of the iris with its attendant evils, but the prompt restoration of the fullness of the globe and of the normal relation of its several parts lessens the chances of irritation from pressure of any cortical fragments or remnants of the capsule upon the delicate contiguous structures and the occurrence of iridocyclitis. In spite of this clear cut statement, the truth of which is generally conceded today we find that suturing of the cataract incision has received considerable attention only within the past 30 years. During the past 30 years many variations in technique have appeared and much has been written enlarging upon Williams' dictum. All this has been to good purpose, for it has made the cataract surgeon so sure conscious that today he does not ask if a

suture is necessary, but he does ask which one is best. In 1937 Ellett presented an excellent review of the subject with a discussion of the various types of sutures employed. It is well to review some of the facts set forth by this author, as they show the trend in "sutures for cataract extraction."

*The conjunctival suture* as initiated by Williams is still widely used. Its chief virtue lies in the ease with which it can be introduced, after the section is completed. Many operators, for instance, Spaeth (48), prefer it for this reason as they want no distracting influence, such as the presence of a corneoscleral suture while making the incision. Since a proper section is so necessary it certainly behooves us to see that the suture does not interfere. If a conjunctival suture is used the flap should be narrow because the elasticity of this membrane is so great that a large flap has practically no splinting effect upon the corneoscleral wound. The experimental work of Hilding is noteworthy, for this worker, using enucleated oxen eyes, made a series of measurements of the intra-ocular pressure necessary to cause prolapse of the iris through limbic incisions under various conditions. From these experiments he concluded that "conjunctival flaps and pockets are essentially ineffective in re-enforcing limbic incisions so as to prevent gaping of the wound and herniation of the iris when healing effects are eliminated." The conjunctival protection of the wound hastens healing but since most iris prolapses occur within the first three postoperative days it is doubtful that the presence of "healing effects" changes the validity of this statement. Leech and Sugar, in their analysis of 450 cataract cases, found that the postoperative complications of (1) prolapse of iris or vitreous or both, (2) delayed closure of the anterior chamber, (3) hyphemia, were much less frequent when sutures were used. The conjunctival suture was found of definite value and the corneoscleral suture of even greater value. Gradual acceptance of the virtues of suturing the wound has led to innumerable variations in technique.

*The corneoscleral suture* Since Kalt, in 1894, described the first corneoscleral suture it seems as if almost every ophthalmologist has attempted to devise some modification of it, until today hardly any two surgeons employ the same technique. Kalt's method has many advocates, among them being Arnold Knapp and Ellett in this country, whose vast experiences certainly justify our giving serious consideration to this form of wound closure. Kalt describes the method of insertion as follows: "The suture consists of a vertical corneal

portion and a transverse episcleral portion. The whole forms a T with a gap between the junction of the horizontal portion with the vertical portion. The length of each of the portions does not exceed 1 millimeter. The vertical intracorneal branch follows the vertical corneal meridian and stops exactly at the junction of the transparent portion with the sclera. The horizontal portion traverses the opaque part of the limbus as near the cornea as possible. An interval of 0.5 millimeter corresponding to the limbus is ample to permit the passage of the knife." Liegard modified this suture by placing both bites horizontally. This type of suture is strongly endorsed by Stallard (49), Leech and Sugar, and others. McLean recently published a description of an effective corneoscleral suture in which after dissecting down a small conjunctival flap a small slot is made at the base of the flap about half way through toward the anterior chamber. A fine black silk suture is then run through the base of the conjunctiva and then through both the scleral and corneal lips emerging in clear cornea just below the base of the conjunctival flap. The increased efficiency of corneoscleral sutures over conjunctival sutures in reducing the number of postoperative complications has been stressed by many (Ellett, Stallard, Lindner) and statistically shown by Leech and Sugar. Among their conclusions were (1) the number of postoperative prolapses is reduced and when prolapse does occur it is smaller; (2) the occurrence of hyphemia is reduced, (3) anterior chambers are reformed earlier, (4) prolapse of the vitreous is eliminated. They also pointed out the advantages of greater postoperative freedom to the aged who with this safeguard can be allowed up within 24 to 48 hours after operation.

Today the indecision rests not upon the value of the corneoscleral suture but upon the best time and way to introduce it. One finds many experienced operators who insert their sutures after the section is completed and others who introduce them before the eyeball is opened. The increased sharpness and delicacy of the atraumatic corneal needles greatly facilitate their introduction after the section is made. However, judging from my experience and observation, sutures introduced at this stage are much less accurately placed and sometimes the operator has to be content with a conjunctival closure, or else run too great a risk in attempting to pick up the sclera. The placing of the suture while the eyeball is still intact is safer although its presence tends to interfere with the smoothness of the section. Nothing must be allowed to interfere with the section, but very little is lost if the suture is severed by the knife.



It can be reinserted upon completion of the section just as easily if not more easily than the original introduction.

**Iridectomy.** The popularity of the preliminary iridectomy has gradually receded, except in England, and today it is used as a routine measure by comparatively few operators. Its usefulness in dislocated lenses was stressed by Wheeler and as he so aptly pointed out these iridectomies should be broad. Many operators, such as Davis (11), O'Connor and Gracie use it only in complicated cases. It seems logical to state that in any case with vitreous in the anterior chamber or when vitreous loss is almost certain to occur its use is definitely indicated.

Although a complete iridectomy at the time of extraction is favored by many competent and experienced operators, notably Knapp, Davis (11), Appleman, and others, the trend is definitely toward extraction with a round pupil. Ellett, Peter Verhoeff, Bracken, and many others have commented upon the advantages of retaining the iris sphincter. Its presence is said to assist in preventing prolapse of the vitreous in the intracapsular extraction and to lessen the chances for capsular and cortical incarceration in extracapsular extraction. It is generally agreed that an iridotomy or peripheral iridectomy lessens the chance of iris prolapse. Hidding's experimental work, previously quoted, showed that an iridotomy opening added to the sclerocorneal suture made it almost impossible to produce prolapse when the opening acted well. This would seem to indicate that the opening to be of value must be large enough to permit free passage of fluid from the posterior chamber to the anterior chamber. The increased frequency of iris prolapse when a round pupil is attempted is not universally admitted but the majority of operators definitely feel that such is the case. A careful pre-operative study of the iris and lens may prove helpful in reducing the occurrence of this complication. A loss of resiliency in the iris from sclerosis, atrophy, adhesions, or any cause tends to increase the chances of iris prolapse. These cases in my opinion should have a complete iridectomy. As Wright (56) has pointed out there is increased difficulty in delivering the lens in its capsule or a large nucleus in extracapsular extraction in the presence of a rigid pupil. In this group he favors an iridotomy including the sphincter in preference to a complete iridectomy. Just 10 years ago Lancaster in an address before this society stressed the advantages of a basal iridectomy over a complete iridectomy. He believes that a basal iridectomy is even better as a preventive of prolapse than a

complete iridectomy pointing out that it prevents capsule complications and at the same time avoids most of the iris complications. Within the past decade the truth of these statements has been appreciated more and more until today the complete iridectomy is no longer a routine procedure but is used whenever the operator encounters definite contra-indications to a peripheral one. Even though comecoidal suturing and consideration of the contra-indications to peripheral iridectomy have materially reduced the number of iris prolapses it is still one of the more frequent complications and its management remains unsettled. Causternization of the prolapse with trichloroacetic acid is advocated by many—Bothman, Gailev, Magitot, Dubois-Ponsen, and Gifford—but others condemn it and suggest excision at the earliest possible moment as the only satisfactory method for curing this condition.

**Selection of operation.** Probably the most striking change that has occurred in cataract surgery within the past 10 years has been the increasing number of advocates of the intracapsular extraction. The extracapsular method is defended especially by Jackson, Moehle, Wright (56) and others, but the number of experienced operators who routinely use the extracapsular extraction is diminishing. Davis (11) for example after using exclusively the extracapsular method for 19 years is enthusiastic over the smooth postoperative course of his intracapsular cases. Gracie believes

"In the hands of the experienced operator the Elschalg method of intracapsular extraction is just as safe if not more so than the older capsulotomy method. On the other hand Pischel after an analysis of a series of cases done by both methods concludes "while the results in the successful intracapsular operation are practically as good as those in the well performed extracapsular operation, there were more bad results even in a selected series of cases of intracapsular operations than in an unselected series of extracapsular operations."

Thus it would seem that the important consideration in cataract extraction is the selection of the proper type of operation. It is not within the realm of this paper to discuss the indications for the intracapsular operation which have been so concisely given by Arnold Knapp who believes, "There is more or less general unanimity in the selection of cataracts that are suitable for this operation. The recent improved methods of anesthesia and other aids have greatly reduced the list of contra-indications. Unfortunately however the tendency has become more and more prevalent to attempt an intracapsular extraction

on almost every case. One often hears that nothing is lost if the capsule ruptures and the lens has to be extracted by the extracapsular method—a teaching which in my opinion should be condemned. We have all had the capsule tear after dislocation has taken place and been forced to deliver as best we can a sticky, partially opaque lens. Under these conditions the removal of the cortical matter by irrigation or by mechanical means is not without added risk and the usual result is that a large portion of it remains. It often lies in the upper part of the anterior chamber more or less in contact with the wound. Secondary glaucoma is not an infrequent sequela. The intumescent cataract which is generally recognized as unsuitable for intracapsular extraction is the most frequent cause of this complication. Similarly failure to consider other contraindications may produce disastrous results.

Within the past 10 years there has been no appreciable change in the technique of the extracapsular extraction, but many articles have been written upon modifications of the intracapsular operation. Without entering into a discussion on the merits of these various methods it is sufficient to say that the technique most frequently employed is the so called forceps and pressure method. No uniformity of opinion exists on the best way to apply the forceps, but the majority believe that they should be used only to control the delivery of the lens which is largely expressed by pressure. Some (Knapp, Peter, Elschsig, and others) insist upon tumbling the lens while others (Beach and McAdams and Verhoeff) apply the forceps above in the equatorial region and extract the lens head on. The cresophake, as designed by Barraquer, has its advocates and many modifications of this instrument have appeared but its use has never become widespread. Saint Martin suggests that it is ideally suited for the intracapsular extraction of the intumescent cataract in which the forceps method is so often unsuccessful—a thought worthy of further investigation, for if we could succeed in extracting these lenses without rupturing the capsule much trouble would be averted.

Wright (56) with an enormous experience of over 20,000 cases correctly sums up the situation in the following words: "Dogmatism in connection with the various procedures of the operative treatment of cataract is not uncommon, as one may judge who follows up current literature, but the greater one's experience the more inclined one is to adopt an open mind. A man may indulge in dogmatism when he has collected figures in connection with 100 cases of the operative treatment of cataract

but he will be less inclined to do so after his thousandth extraction and completely alter many of his previous views after his five thousandth case." There are few if any of us who will ever perform such a vast number of cataract extractions. Nevertheless the truth of this statement can not be denied. Let us, therefore, realize that there are indications for the extracapsular as well as for the intracapsular extraction and strive constantly toward a perfection of these indications.

# REFERENCES

- 1 APPLEMAN, LEIGHTON J. Intracapsular cataract extraction. *Arch Ophth*, 1938, 19 548-554.
- 2 ARRUGA, H. Les détails techniques de l'extraction intracapsulaire du cristallin. *Bull et mcm Soc franc. ophth*, 1933, 46 270.
- 3 ATKINSON, WALTER S. Local anesthesia in ophthalmology. *Tr Am Ophth Soc*, 1934 32 399-451.
- 4 BARTELS Die Staroperation aus der Kapsel und in der Kapsel. *Klin Monatsbl f Augenh*, 1937, 98 815-816.
- 5 BEACH, S J, and McADAMS, W R. Intracapsular extraction of cataract in the average practice. *Arch Ophth*, 1936, 15 95-100.
- 6 BERENS, CONRAD, and BOGART, DONALD. Certain postoperative complications of cataract operations. *Tr Am M Ass, Sect Ophth*, 1938, pp 238-283.
- 7 BOTHMAN, LOUIS. Repair of rupture of the wound after extraction of cataract. *Arch Ophth*, 1937, 17 1073-1075.
- 8 BRACKEN, F. Intracapsular extraction with indotomy, 100 successive cases with capsule forceps. *New York State J Med*, 1938, 38 610-615.
- 9 BURTON, ROBERT. The intracapsular extraction of cataract with forceps, is it justifiable? *Brit J Ophth*, 1930, 23 505-539.
- 10 DAVIS, F A. Tribromethanol as an anesthetic in eye surgery. *Tr Am Ophth Soc*, 1931, 29 47-74.
- 11 Idem. Personal experiences with intracapsular cataract extractions. *Arch Ophth*, 1938, 19 867-881.
- 12 ELLETT, E C. Use of the suture in extraction of the cataract. *Arch Ophth*, 1937, 17 523-529.
- 13 FLSCHING Staroperationen kritischer Bericht ueber das Schrifttum 1934 bis einschli 1935. *Zentralbl f d ges Ophth*, 1938 43 321-340.
- 14 FRANCESCHIETTI, A. Die Livpannatnummernose bei Augenoperation. *Klin Monatsbl f Augenh*, 1934, 93 106.
- 15 GALLI, WATSON W. Some problems encountered in cataract surgery. *Am J Ophth*, 1935, 21 855-864.
- 16 GIFFORD, SIVJORD R. Prevention of complications in cataract operation. *Illinois M J*, 1935, 68 243-245.
- 17 GIL, R R, and QUEPOL, A G. La anestesia con el evipan sodico en cirugía oftalmológica. *Arch de oftal de Buenos Aires*, 1936, 11 601-607.
- 18 GOW, LYNN. Management of the complications of intraocular surgery. *Am J Surg*, 1938, 42 62-65.
- 19 GRADLE, HARVEY S. Intracapsular versus extracapsular extraction of cataract. *Am J Ophth*, 1934 17 497-501.
- 20 GRAVES, BASIL. Cataract and other operations during deep sleep induced by paraldehyde and omnipon. *Tr Ophth Soc U Kingdom*, 1938 49 307-306.
- 21 HARTSHORNE. Comparison of intracapsular methods of cataract extraction. *Am J Ophth*, 1935, 19 305-307.

2. HERRINGHOWARD, F. v. Die Wendeprengung nach Altemstar Extraction und ihre Verhütung durch die Anlegung eines vorbereiteten Blindes klappen. *Zschr. f. Augenh.* 934, 83, 87-94.
3. HILLMAN, ALBERTUS. Efficiency of various suture closures in prevention of prolapse of the iris after cataract operations; experimental study. *Arch. Ophth.* 939, 177-92.
4. JACKSON EDWARD. Applied mechanics of cataract extraction. *Am. J. Ophth.* 938, 30-4 6.
5. KALT, E. On the corneal suture in cataract extraction. *Arch. Ophth.* 894, 3 4-4 3.
6. KARFENKIRCH, M. W. Sur l'akéomé. *Bell. et. méém. Soc. franc. ophth.* 934, 47 92.
7. KELLIE, M. Survey of different methods of suture closure after cataract operation. *Tr. Ophth. Soc. U Kingdom*, 936, 59, 893-905.
8. KNAPP ALBINO. Certain aspects of the intracapsular extraction of cataract by forceps. *Arch. Ophth.* 936, 6 4 9-44.
9. KNAPP H. On cocaine and its use in ophthalmic and general surgery. *Arch. Ophth.* 1834, 3, 407-443.
10. KUNKE, J. Die operativ und konservative Behandlung des Altemstars. *Zentralbl. f. d. ges. Ophth.* 935, 3, 432-45.
11. LANCASTER WALTER. The cataract operation. *Surg. Gynec. & Obst.* 93, 5, 452-463.
12. LA AL, JOSEPH. Avertin anesthesia for ophthalmic operations. *Arch. Ophth.* 938, 9, 7 4-7 8.
13. LEACH, V. M. and SCOUR, H. S. Reduction of post operativ complications in cataract operations with cornecolateral sutures. *Arch. Ophth.* 939, 966-975.
14. LEZARD, H. Une modification au procédé de suture de la cornée dans l'opération de la cataracte. *Ann. d'ocul.* 9 3, 149 9- 86.
15. LINDSTER, K. Rühmeser zur Anlegung einer Vorhaut bei Staroperation. *Zschr. f. Augenh.* 936, 90, 237.
16. LOEWENSTEIN, A. Zur Indikation und Technik der intrakapsulären Staroperation. *Klin. Monatsbl. f. Augenh.* 938, 440.
17. MAGGIORI A. and DUBOIS-POULET, A. Traitement des prolapsus iriens par l'acide trichloracétique. *Technique de Bettman et Barham. Ann. d'ocul.* 938, 75, 440-454.
18. MCCOY, J. L., and DICKER, C. A. Intracapsular extraction of senile cataract. *Calif. & West Med* 935, 43, 800-807.
19. MCLEAM, JOHN M. A new cornecolateral suture. *Arch. Ophth.* 940, 3, 354-359.
20. McREYNOLDS, J. O. Management of complications in operations for cataract and glaucoma. *Surg. Gynec. & Obst.* 936, 6, 517-5 9.
21. MORGAN, WALTER. Cataract extraction through vertical conjunctival slit. *Arch. Ophth.* 1936, 16, 659-66.
22. O'NEILL, C. S. Alkalis during cataract extraction. *Arch. Ophth.* 939, 447-449.
23. O'CONNOR, ROBERT. Cataract extraction by the unattached conjunctival bridge method after preliminary iridectomy. *Am. J. Ophth.* 934, 7, 809-8 7.
24. PETER, LUTHER C. Intracapsular cataract extraction: the relative merits of the modern methods and indications for their use. *T. Am. Acad. Ophth. & Oto-Laryngol.* 933, 38, 90- 9.
25. PRINCE, DOMENICO. A. Comparative and results in the intracapsular and extracapsular operations for the removal of senile cataracts. *Am. J. Ophth.* 934, 17, 326-33.
26. DE SAINT MARTIN, R. Prospects of the intracapsular extraction of cataract. *J. Modern Trends in Ophthalmology* p. 505-608. Edited by F. Ridley and A. Bonny. London: Butterworth, 940.
27. SEATER, EDWIN B. Discussion of Dr. Luther C. Peter, loc. cit.
28. Idem. Principles and Practice of Ophthalmic Surgery p. 56. Philadelphia: Lea and Febiger 939.
29. STALLARD, H. R. A. Corneo-scleral suture in cataract extraction: its technique and advantages. *Brit. J. Ophth.* 938, 269- 73.
30. URBACHER, J. and ALLEGRETTI, W. C. Hämio und Lebensdauer. *Klin. Monatsbl. f. Augenh.* 937, 90, 934-935.
31. VAN LEST, Farah sie palpebrale temporaire protégée dans l'opération de la cataracte. *Ann. d'ocul.* 934, 51, 420-424.
32. VERNHOUT, I. H. Discussion of Beach and McAdams, loc. cit.
33. VOGT, A. Demonstrationen zu Verbesserungen in der Technik der Staroperation. *Schweiz. med. Wchschr.* 935, 6, 949-95.
34. WILLIAMS, HENRY W. Cataract extraction operations. *Arch. Ophth.* 860, 95- 2.
35. WRIGHT, MONTEY E. Blocking of the main trunk of the facial nerve in cataract operations, based on experience of over 30 cases. *Arch. Ophth.* 936, 55, 533-539.
36. Idem. Lectures on cataract. *Am. J. Ophth.* 937, 20, 9- 3, 240- 53, 376-387.

# THE 1940 CLINICAL CONGRESS

## THE COLLEGE AND AMERICAN SURGERY

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A PRESIDENTIAL address in my opinion should give an account of the affairs of the organization, an accounting for stewardship as it were. The American College of Surgeons is fortunate in having a splendid organization with minute and detailed reports available, and hence its president has but little to do. Therefore, it seems to me that this address might serve to welcome the initiates who shortly will become Fellows of the College and also to discuss certain details of the College, its aims, and objectives.

Most of the successful ventures in human endeavor come from organization and we think this is particularly true of medicine. The labor union exists for the purpose of improving the economic status of its members, the medical association or college exists to improve the scientific attainments of its members by organized effort.

The foundation of the American College of Surgeons sprang from an idea. In 1903, the Society of Clinical Surgery was organized for the purpose of demonstrating to a group of surgeons the methods used in different leading clinics. The effort was most successful and naturally as surgeons from different cities watched each other work, they were bound to carry home with them the best of the surgical procedures they had observed. Apparently this gave to Franklin Martin, of Chicago, the idea of organizing a greatly magnified and practical clinic.

In 1910, in Chicago the Clinical Congress of Surgeons of North America was organized, and 1,300 surgeons were in attendance. The organization was rather loose and Martin, with characteristic foresight, saw the possibility of banding these men together in an organization which would stand for the uplift of surgical principles and technique and practice. Hence, he formulated the organization of the American College of Surgeons in 1913, and after a founders' group had been formed, 1,059 initiates were enrolled into fellowship at the first Convocation.

In the Articles of Incorporation it is stated that the object for which the American College of Surgeons is formed is

"to establish and maintain an association of surgeons, not for pecuniary profit but for the benefit of humanity by advancing the science of surgery and the ethical and competent practice of its art, by establishing standards of hospital construction, administration, and equipment, and all else that pertains to them, by engaging in scientific research to determine the cause, nature, and cure of disease, by aiding in better instruction of doctors, by formulating standards of medicine, and methods for the improvement of all adverse conditions surrounding the ill and injured wherever found. To accomplish these benevolent and charitable aims, it shall be within the purposes of this corporation to use those means which from time to time may seem to it wise, including research, publication, education, the establishment and maintenance of libraries, museums, and other agencies or institutions appropriate hereto, and the co-operation of any other such activities, agencies, or institutions already established or which may hereafter be established."

Whoever wrote these sentences wrote a masterpiece because in the twenty-seven years since its organization the College has done every one of these things.

The historic position of the early beginnings of the American College of Surgeons is somewhat different from that of other colleges then in existence. Conforming to the democratic principles of this country, its fellowship was considered inclusive, not exclusive, and it was to be conferred upon surgeons of character, honesty, and ability without particular regard for examination. Certain simple standards were set up, but the supreme test was the recognition of the candidate's fitness by a group of surgeons, Fellows of the College, who knew him best because they worked together in the same community. Therefore, from the beginning the opinion of the State or Provincial Credentials Committee was the dominating influence against the admission of those known to be incompetent or unethical.

It is not so difficult to judge a man's knowledge of the theory and technique of surgery by examination as it is to know that he can apply this knowledge to the individual patient, it is important to know that the surgeon is able to work in a community without friction with his colleagues,

Presidential address of the retiring president presented before the Clinical Congress of the American College of Surgeons, Chicago, October 1-5, 1940

and it is most important to know that he is honest in his relations with the patient. The College makes every effort possible to combat the evil of fee-splitting and while it may not be an issue in all communities and in all hospitals, it has been necessary to establish a uniform regulation to avoid discrimination and to require the medical staff and governing board of every hospital desiring approval to go on record against this practice. Once on record, it is the duty of the hospital management to exercise continuous vigilance to prevent fee-splitting under any guise. The pledge against the division of fees, which is signed by all Initiates, was proposed by Dr. Albert Ochsner in Chicago in 1913.

The meeting held each fall is the high point of our College year. The program consists of papers and discussions, of clinics and operations, all illustrative of the progress of the surgery of the day. Those who formulate the program endeavor to give the meeting the benefit of the master minds of surgery. If you would take the time to examine the Clinical Congress programs through the last twenty-seven years, you would read an epitome of the progress of surgery in this country.

In 1910, the College began to organize three or four sectional meetings in different parts of the country each year. They have grown in time so that they almost rival the fall meeting and have been of immense aid in establishing contact with the Fellows of the College.

In a way these meetings are something like other medical meetings, except that they are better and hence it is necessary to look further for the great influence of the College. When we do so we realize that we are part of a great organization exerting a power by the force of our numbers for the good of surgery. If for no other reason, you should be satisfied with your fellowship because, after all, that which concerns the good of surgery as a whole concerns each one of us.

At an early date it was recognized that the hospital and operating room were the laboratories of the surgeon and that many hospital organizations were careless regarding the equipment, the records, and the laboratory facilities. By 1917, the hospital standardization program was well under way and despite the hectic years of the World War our program was developed and a minimum standard for hospitals was adopted in December 1917. Beginning in 1918 the College began a survey of the hospitals of the United States; these surveys have been made every year since until over 3,600 hospitals are now on the survey list and are regularly visited by members of the College staff.

In 1913 at the suggestion of Dr. Thomas Cullen, of Baltimore, a cancer committee was appointed that subsequently formed the nucleus of the American Society for the Control of Cancer. Later the College took over the bone sarcoma registry and in 1922 began assembling data of all cancer cases living five years or more after treatment. The College then established a minimum standard for cancer clinics and organized them in approved general hospitals. Today there are 345 approved cancer clinics.

In the same year under the guidance of Dr. Charles L. Scudder of Boston, exhaustive studies of the present treatment of fractures were conducted and the central fracture committee and regional fracture committees in different states and provinces have become one of the most important duties of the College.

In 1916, we organized a board on industrial medicine and traumatic surgery which concerned itself with adequate scientific and ethical care of the ill and injured in industry and this committee, although now fused with the fracture committee has had a beneficial influence and has made many contacts with the large industrial concerns.

From the beginning Canada was included in the organization of the College and in 1920 and subsequent years, Drs. Franklin Martin, William J. Mayo, Thomas Watkins, and others visited the various South and Central American countries, thus binding the surgeons of these countries to the College so that it could be said to be representative of both Americas. As a result of these contacts and because of the standardization program of the American College of Surgeons, Dr. Francis P. Corrigan, now the United States Ambassador to Venezuela and an enthusiastic Fellow of the College, paid a great tribute to the College in his article *El Libro del Hospital Moderno*.

The influence of the College was recognized during the first World War when President Wilson appointed Dr. Franklin Martin one of seven civilians to the Advisory Commission of the Council of National Defense. This year Dr. Evans A. Graham, president-elect of the College, has been appointed chairman of the National Research Council Committee on Surgery in connection with the program of military preparedness. The chairman of our Board of Regents, Dr. Irvin Abell, has been appointed chairman of the Committee on Health and Medicine of the Council of National Defense. At the Clinical Congress held in October 1917, the program was indeed a 'war session' and while we are not at war you will notice from the program of the present meeting that we are preparing for defense.

It is interesting to me to note the duplication of thought about the two wars. The high point in the treatment of wounds in 1918 was the Carrel-Dakin irrigation, today it will be sulfanilamide. There will be many improvements in transportation, but I think that the basic surgery will be comparable. There is not a great deal of information in the medical literature of the past year regarding the surgical aspects of the war, yet all surgeons liable to service in the event of war prepare themselves by searching every available source for information regarding the treatment of wounds and other war casualties and the hazards of industry in the conduct of war. As a matter of fact, in a total war, every doctor and every hospital is an integral part of the defense plan.

In his presidential address of last year, Howard Naffziger compared medical progress to a growing stream, the first spring feeding it arising in the far distant past until with the development of modern scientific medicine the stream has become a great river. I do not think it possible to say when and where surgery began because no doubt from the dawn of civilization and even before men attempted to alleviate suffering and injury by some form of material help. At any rate, we do know that much of the practice of surgery began in mystery and magic.

The earliest surgical operation which history records was the trepanning of skulls for the release of demons, presumably the epileptic seizures of the present day. Bloodletting began as a ceremonial procedure. Circumcision was practiced in 4,000 B C according to the picture record and the records in Genesis. In time superstition in medicine disappeared but, despite the enlightening developments of Galen and Celsus, surgery remained in the doldrums until Vesalius early in the sixteenth century taught true anatomy.

Often we hear of an attempt to distinguish between the art of medicine and the science of medicine. Actually, medicine is not a science but gathers its basic knowledge from true science and applies it to the cure of disease, and hence, after Vesalius, anatomical thought ran like a red thread through all of the developments of medical practice. In 1628, eight years after the landing of the Pilgrims, William Harvey announced the theory of the circulation of the blood, thenceforth physiology was inseparably associated with anatomy and surgery became more exact. Harvey taught that speculation alone was valueless, that advances in knowledge would result only from patient experiment, patient measurement, patient application of the method of trial and error, and

that the facts, if they were facts and if there were enough of them, would always speak for themselves. Patiently through the years the science of physiology unfolded its secrets to medicine until today we constantly talk in details of function, and surgery endeavors to restore normal function or to remove an offending organ.

Sometime in the eighteenth century the pupils of the great chemist, Robert Boyle, discovered the different gases in the atmosphere and thus led to the discovery of inhalation anesthesia, the word "anesthesia" having been invented by Oliver Wendell Holmes. In 1584, Fracastorius wrote that contagion is infection passing from one individual to another. Step by step the picture was completed with Holmes, Semmelweis, Pasteur, Koch, and Lister standing out in the foreground. From the time when Lister developed the technique of antiseptics in 1865, surgeons were concerned with methods which combined antiseptics and sterilization by heat and allowed operations to be undertaken safely with ever increasing freedom.

For a long time there was not much progress except the perfection of details for fulfilling the doctrine of antiseptics. In 1910, Ehrlich produced salvarsan and this discovery not only revolutionized the treatment of syphilis but exerted such a stimulus to chemotherapy that today most progress in surgical technique is closely allied with the progress of chemical research.

Surgery benefited from the field of physics when in 1895 Roentgen discovered x-rays. The efficiency of this instrument of diagnosis and treatment has progressed until today, judging from reports which we hear, we may be on the verge of extraordinary developments by the use of the cyclotron. After Roentgen came the Curies and the isolation of radium, and its use particularly in cancer was another step forward.

These few remarks are introduced merely to furnish a backdrop to the stage on which is played the drama of medical progress. Scientists have discovered so much and the application of their discoveries have complicated medicine so that specialization has developed. For a long time physicians combined the art of general practice with the practice of a specialty. But with the great advances in medicine and science we have come to realize that major surgery is a complex procedure, requiring not only a knowledge of technique but a sound understanding of the principles of anatomy, physiology, pathology, chemistry, and physics.

In the past special training was obtained largely through the personal initiative of the physician

A period of study abroad was considered necessary and Paris, Berlin, and Vienna were popular mecca for medical students. Courses were given in this country by certain postgraduate schools, but with the exception of the one at the University of Pennsylvania established in 1919, these courses were largely short in duration and rarely satisfactory. Most surgery was taught by the preceptorial method. The younger men became associated with established surgeons as assistants and gradually learned the technique of surgery. As the technique of surgery became magnified, it was realized that the training of the general surgeon and the surgical specialist would require more time and effort on the part of the individual. For many years there have been opportunities for surgical training in the medical school hospitals and in a few other institutions, but it was becoming apparent that the need for training exceeded the good available opportunities. The College realized that in its hospital standardization surveys it had the machinery to increase the opportunities for graduate training in surgery and the surgical specialties. The subject has received the continuous consideration of the Board of Regents since 1930 and several committees have studied the problem in its relations to the requirement for fellowship. During the past three years the committee on graduate training in surgery and the field staff of the College have done a great piece of work and we can announce that 200 hospitals and other medical institutions are participating in approved plans of graduate training in general surgery and the surgical specialties at the present time.

It is interesting to philosophize on the question as to what is a surgeon. In his presidential address read before the American College of Physicians last April, Dr O. H. Perry Pepper attempted to answer the question, "What is an internist?" He found himself involved in a quagmire of words and meanings and definitions and finally concluded that

"an internist is—physician fitted by sound and applicable knowledge of the basic sciences, continued training in clinical medicine, familiarity with facts outside his own, and an intellectual, rather than manual or technical, approach to study, diagnosis, and treatment of the diseases of the field of internal medicine to which he strictly limits himself and to integrate with the knowledge of his own field that of the allied specialties.

With some change in phraseology this definition might define the surgeon. Much of surgical procedure is done and rightly so, by the general practitioner but a borderline is soon approached when the performance of a major operation on the

brain, the chest, the abdomen or the extremities involves not only manual skill but also a knowledge of anatomy pathology and the other basic sciences together with a group of the increasingly difficult problems of pre-operative and postoperative care. The surgeon therefore, cannot be a general practitioner. He must have time to read, to study and to observe the work of other surgeons and unfortunately cannot cultivate the personal and family psychology of the patient as can the general practitioner to whom he is consultant and ally.

The formation of the boards of certification has influenced the desire for residencies, and the trend of present opinion is that such a residency is necessary for adequate training in surgery.

"There is gentle irony in the fact that men who to large extent are self-taught believe that their successors cannot achieve an education in the same manner."

One of the problems of the future should be a study of the effect of prolonged residencies on medical education on hospitals, and on the practice of medicine. This movement is formulating

very difficult problem for the hospitals because much of their organization must be dislocated in order to accommodate the new and important links between the interne group and the visiting group. Staff members and boards of trustees must be convinced of the importance of the residency and must be persuaded that sacrifice may be necessary to make it effective. The senior visiting staff must assume a preceptorial attitude and regard themselves as graduate professors of surgery. The junior visiting staff is in danger of being squeezed out from above and below unless the adjustment is made so that they also take part in the training plan.

In due time the new system will produce more highly trained men. A present day problem as well as one for the future is to formulate methods or backgrounds that will enable the individual trained in the residencies for two, three, or four years to adapt himself to competitive medical practice. As the *New England Journal of Medicine* states, these men will start with a strong tendency toward group medicine rather than toward individual practice.

I think that now I have said enough and really have said little but perhaps have offered some points for analysis. In 1874 Sir John Erichsen stated that "the abdomen, the chest, and the brain would be forever shut from the intrusion of the wise and humane surgeon. Unlike Lister he failed to envision the effect of Pasteur's germ theory upon the surgical operation. The researches

in chemistry today seem to us to be revolutionary in their effect upon the treatment of disease, but our sons and our grandsons will develop other ideas which will be thought to be the extreme in modern methods. Unlike Erichsen, we must not

exclude any lesion or organ as immune from surgical attack. And then we might look forward to the time when medical science has progressed to the point when all surgery of a destructive type can be abolished.

## MEDICINE IN THE NATIONAL DEFENSE PROGRAM

IRVIN ABELL, M D, F A C S, Louisville, Kentucky

SINCE the members of the American College of Surgeons, with the exception of the Canadians present, are practically all members of the American Medical Association, I felt that you would be interested in knowing of the work of its Committee on Military Preparedness. This committee was appointed at the session of the House of Delegates in New York in June following a request of the Surgeons General of the Army, Navy, and Public Health Services that the American Medical Association undertake a survey of the profession of the United States regarding the qualifications and availability of its members for service.

There are 179,000 doctors entitled to practice in the United States by means of legal registration, and a questionnaire was sent to each of these. Between 140,000 and 145,000 are in active practice, while the remainder have retired because of age, disability, or their having sought other pursuits. So far 115,000 replies have been received, of which over 50,000 have been transferred to punch cards. These punch cards contain the information furnished by the questionnaires and by using them in the International machine, one may in a few minutes get a list of men qualified in any branch of medicine. This work has been undertaken by the American Medical Association as a patriotic contribution to the National Defense Program and has entailed the employment of an additional sixteen persons in the American Medical Association office. It is hoped that within two or three months information will be at hand upon every doctor in the country. The only exemption in the Selective Service Act applies to students of theology and accredited ministers of the gospel. Deferments will be made to students in accredited schools, pursuing a course of study leading to a degree in

Arts and Sciences and also to those who occupy essential positions in their community. In order effectively to safeguard the health of the population and to furnish medical service to the armed forces, the medical profession feels very strongly that medical students should be permitted to finish their undergraduate education and, at least, one year of internship before being inducted into service. The Selective Service Act, however, provides deferment for students only until June, 1941, after that date any deferment granted to medical students, to internes, and to residents will be the responsibility of the local draft boards. While doctors should be willing to make such adjustments as may be needed in the event of an emergency, it would be unfortunate if in the defense program the classes of medical schools, the teaching program of medical schools, and hospital service should be disrupted by an undue number of students, of internes, and of residents being called into service. This can be avoided only by applying to the local draft boards and to the appeal boards for the deferment of those essential to these three activities.

There are approximately 15,000 members of the Medical Reserve Corps and these will be largely drawn upon to furnish medical service for the first increment of selectees. It is estimated that by July, 1941, the total strength of the Corps will be approximately 1,400,000 members and the services of 10,000 doctors will be required. The length of service of the vast majority of doctors will be one year, at the end of which time they will be transferred to the Reserve Corps on an inactive status. The information being gathered by the Military Preparedness Committee of the American Medical Association will make it possible to employ the number of doctors in position for which their training and qualifications fit them, and thus to avoid some of the mistakes and misfits of the First World War.



The major objectives of the survey are to provide medical service for the armed forces, to provide medical service for industrial mobilization, and to provide continuing medical service for the civilian population. In the first World War more than 32,000 physicians voluntarily served with the armed forces. In the event of war coming to our country again the profession will similarly give of its members a sufficient number to meet the needs of the Army, Navy, and Public Health Service. Furnishing medical service to the rapidly expanding industrial plants presents many difficulties. It will be no task to supply doctors who are fully competent to care for industrial injuries, but it is quite another problem to supply doctors familiar with the toxicological problems of industry. Practically all of the metals, many of the solvents, benzol, tulzol, and many chemicals used in industry are capable of producing rather disastrous toxic effects upon the human organism. To control these hazards effectually requires the co-operation of the physician who is familiar with the problems and the safety engineer who understands methods of prevention. Continuing the service to the civilian population through hospitals and through men in various fields of practice is essential if the health and welfare of the civilian population is to be protected.

On September 19 President Roosevelt appointed a Health and Medical Committee a sub-committee of the National Defense Council. Its mem-

bers are Surgeon-General Magee of the Army, Surgeon-General McIntire of the Navy, Surgeon-General Parran of the United States Public Health Service, Dr. Lewis H. Weed, chairman of the Division of Medical Sciences of the National Research Council, and your humble servant, representing the civilian profession. The duties of this committee are to advise the National Defense Council on health and medical matters affecting National Defense and to co-ordinate all health and medical efforts. The medical division of the National Research Council has at present 35 committees, each studying some problem in its relationship to military medicine, such for instance as shock, chemotherapeutic treatment of wounds, blood transfusion aviation medicine, tuberculosis, neuropsychiatry nutrition etc. The Health and Medical Committee has appointed sub-committees on dentistry, medical education hospitals, nursing, industrial health and medicine, and negro health. In all of this work an effort has been made to secure the advice and help of those whose qualifications in their respective fields entitle them to serve with advantage to the country.

It gives me much pleasure gratefully to acknowledge the unanimous offer on the part of the profession at large, of the various national and special medical societies, of the hospital groups, in fact, of all agencies relating to health and medicine to co-operate fully and freely in the defense program.

# THE CIVILIAN SURGEON IN WAR

Brigadier General RAYMOND F METCALFE, M D , F.A.C.S , Washington, D C

**B**EFORE proceeding with a discussion of conditions in the Army which the civilian surgeon would encounter in the event of a general mobilization, I should feel remiss if I failed to pay tribute to the brilliant accomplishments of a few of our Army medical officers. Major Walter Reed and his associates showed us how to control and practically eradicate yellow fever. Colonel F F Russell, encouraged by Surgeon General O'Reilly, with great persistence and hard work secured volunteers to submit to antityphoid vaccine, proving it worthy as a preventative, and thus typhoid fever was practically eliminated from the Army where formerly it took a greater toll of death than battle casualties. There are many young medical officers in the Army today who have never seen a case of typhoid fever. Surgeon General William C Gorgas, through his knowledge of sanitation and prevention of yellow fever and control of malaria, made possible the construction of the Panama Canal. The work of Colonel William L Keller in the first World War on empyema cases following wounds and pneumonia is the real basis for all the brilliant present day thoracic surgery. Colonel Keller contributed another important contribution to war time equipment—the "Keller half ring splint," which has completely replaced the Thomas splint in the Army. The Keller splint is reversible and can be used on either right or left leg. After the splint has been padded, the damaged leg is laid in it and the half hip ring is completed to a full ring by a strap. The Thomas splint with a full hip ring can be used only on one side, thus twice as many splints are required. They are much more awkward to store and transport, are more difficult to apply as the injured foot and leg have to be passed through the ring, thus causing unnecessary manipulation of fractured bones.

From the Surgeon General's Office U S Army  
Presented before the Clinical Congress of the American College  
of Surgeons Chicago October 21-25 1940

Since this paper was written, early in August, 1940, a considerable portion of the National Guard has been mobilized for defense of the United States. Usually the Guard is called by regiments and the medical officers and enlisted men of the medical department are included. If one million men are mobilized by the selective draft that means seven thousand medical reserve officers will be called for service.

Many of the medical men here served with the Army during the first World War and are familiar with service conditions, and while we all hope that war will not be forced upon us the best insurance against such an event is a well trained and equipped army. I do not believe we will have to maintain a regular army of two million men permanently. Yet, we should have five to ten million men trained in the use of small arms and field guns, airplane pilots, tank drivers, machine gunners, signal corps men, and trained x-ray, laboratory, pharmacy, and dental technicians, as well as men trained in administering first aid.

The only way this can be accomplished will be by the establishment of a selective draft or universal service. The latter is the more equitable method. Every youth from 18 to 21 years of age, physically qualified, could, with advantage to himself and the Government, give 1 year to the Army, Navy, or Marine Corps, and thereafter for a determined number of years serve 14 days yearly with the colors.

If you could observe some of the recruits—awkward, with ungainly walk, round shouldered, and with faulty and unsanitary habits—after a 6 weeks' training period change into upright, alert, self-reliant, and well disciplined young soldiers, I am sure you could not offer a legitimate objection to the selective draft or universal service. Their improved health and physique more than offset any interruption to education, their improved physical condition and response to discipline work to their benefit throughout life. After a few years of

this training, with the spirit and intelligence of the American youth, it would be a bold people who would start trouble with the United States.

The younger medical officers assigned to duty with troops must remember that most of the recruits and draftees face a complete change in their mode of life. Their army life is regulated and the change in their habits is very marked. They are awakened by a bugle call, have a very short time to wash, shave, make up their beds, take a setting up drill, go to breakfast shortly afterward, are called to drill again, and this routine continues during the day. At night they are summoned to quarters with a call for lights out at 9:00 P.M. With this regulation of his life the recruit may neglect the calls of nature and feel ill. The sergeant puts his name on sick book and when sick call is sounded he and others of his company are marched to the doctor's office at the dispensary or hospital. With a large number of recruits, 50 to 100 men may have to report to the medical officer whose duty it is to see each man and find out his complaint. The sergeant, of the medical department, is instructed by his superior officer to take temperatures when indicated, to examine an injury or otherwise take care of the men. To many a dose of salts will be prescribed to some a cough mixture, and these recruits will be marked "duty." Some will be detained until the doctor can examine their abdomens, since by change of habits many men become constipated, we must always be suspicious of appendicitis and must not give cathartics when a man has pain in the abdomen. Again, the chest must be examined, and it must always be remembered that, with recruits from country districts especially measles, mumps, and meningitis must always be watched for and the men isolated in the hospital, for it is better to isolate them on suspicion of an infectious disease than to wait for many others to be exposed.

The line officers and drill sergeants who are responsible for the efficiency and the discipline of the recruits often speak sharply and with a good intentioned oath. Sometimes the new medical officer tries to emulate his brother officer of the line thinking the recruit is

malingering and often the new soldier is not seriously ill, just tired, a little constipated, and homesick. The medical officers should be firm but kindly. A little sympathy and friendly advice will help a lot. If there is any doubt of illness, better err by sending the man to quarters or the hospital for a day than to wait until he becomes seriously ill. Remember the medical officer and the chaplain are the only officers who can show a little sympathy for the new soldier without lowering discipline. Also remember that, with large concentrations of men, measles is often the first serious condition, followed by pneumonia, then empyema. This disabling sequence may be stopped by prompt isolation of the measles patient.

The American Medical Association has rendered a splendid service by card-indexing the physicians and surgeons of this country with their specialties and qualifications. This index will enable your Government to call on those needed for various assignments. It is often a hardship on a medical man temporarily to leave his practice yet it will be necessary for all of us to help the Government maintain itself and I am sure no American born or any adopted by America would care to give up his privileges and opportunities to lead the life he has chosen for that of a totalitarian form of government.

In war the country is divided into zones. That portion where fighting occurs, both land and water is known as the combat zone. Behind this section, where supplies are brought forward and wounded taken back, is the zone of communications, and farther back, the zone of the interior where conditions are more or less normal except for the busy factories making supplies for the Army recruiting, and distributing supplies and caring for the sick and wounded.

The first medical installation in the combat zone where the wounded may receive medical attention is the battalion aid station. This is close behind the firing line. Here, the battalion surgeon with meager equipment can apply a splint to a damaged arm or leg, give a hypodermic of morphine, antitetanic serum, apply a tourniquet and a moderate sized dressing.

Behind the battalion aid station are 3 collecting companies, each with 1 medical officer and 31 litter bearers. The non-ambulant wounded are carried by litter to the collecting station, preferably located behind a ridge or behind wooded land, where they will be protected from direct gun fire. To this point the ambulances proceed and take 4 litter patients or 2 litter and 6 sitting patients per ambulance. The ambulances take their patients to the clearing station, here are 6 medical and 1 dental officer with 95 medical department enlisted men. Also, there is a moderate equipment of field operating tables, medical chests of dressings, instruments, splints, equipment to furnish hot drinks, warm blankets, intravenous fluids. There is also equipment for such emergency operations as removal of hopelessly shattered arms and legs, removal of tourniquets and ligating vessels, application of more substantial splints to fractured arms and legs, removal of cloth or foreign material from sucking chest wounds, suture of the skin and fixation with adhesive straps, adjustment of bandages, suture of gaping abdominal wounds and, if the bowel is perforated, exteriorization of the loop and the application of dressings.

This station is equipped with the following anesthetics: inhalants, ether, intravenous, pentothal sodium, infiltrating, procaine and novocain, local, cocaine for eye and mucous membrane.

The commanding medical officer will have to estimate the patient's condition and decide where he is to be evacuated. At this time I wish to mention the work in 1936 of Major Sam Seeley with Drs. Essex and Mann (1) of the Mayo Clinic. When animals were given ether anesthesia and the peritoneal surface of the bowel was irritated by rubbing with gauze, they went into shock in 3 to 3½ hours. When these animals were given pre-operative sodium amytal, shock was delayed 10½ hours. We have observed in our spinal anesthetics, which are all preceded by sodium amytal or nembutal, that we rarely have a shocked patient. With this observation and the result of the animal experiments mentioned, we recommend that the battalion surgeons and hospital corps men be equipped with sodium

amytal capsules 0.2 gram and 1 capsule be given to every seriously wounded soldier before he is started to the rear. If shock is delayed 10 to 11½ hours, the safe evacuation by air or ground ambulance to fixed hospitals in the rear will mean the saving of many lives. Even shocked patients will not recover unless their surgical conditions are corrected. The next station is the evacuation hospital. Here débridements and all type of regional surgery can be done. If a patient can stand ambulance transportation, he should be sent to the evacuation hospital. For the more seriously injured the ideal method of transportation from the clearing station will be immediate evacuation by motor ambulance to a landing field, thence to the base or general hospitals in the zone of the interior by airplane ambulance. A dying man should not be removed from the clearing station.

Translation of "Casualty Evacuation by Airplane" in the Army Medical Bulletin No. 53 (2), based on German experience in Poland, is interesting, as it is probably the first time that battle casualties have been evacuated by air. Lieutenant General Erich Hippka, surgeon general, German Air Force, reports that 2,500 patients were evacuated by plane from Poland to hospitals in Berlin and elsewhere.

Ordinary commercial passenger planes were used. The plane is easily arranged for litter transport by straps and brackets to steady litters. An experienced medical officer in charge and available oxygen is required. The recumbent position lessens danger of air sickness, this rarely occurs under an altitude of 1,000 meters and if greater altitudes are necessary, oxygen relieves. No prolapses of organs or marked disturbances of peripheral circulations were reported. A final opinion of transportability of thoracic injuries was not rendered. Brain and face wounds, eye injuries and shattering wounds of spinal column, pelvis, and extremities were particularly favorable for air transportation *before* operation. Dysentery and typhoid patients were transported by air to home hospitals. Motor ambulance transport is necessary at the front and the home base to and from landing fields. The return journeys of the planes carried sera, medicines, and required equipment to the

front. Of the 2 500 evacuated by plane only 4 patients died in plane or immediately after landing and these planes were not staffed by medical officers. The speed of the ambulance planes was maintained at around 144 miles per hour. All planes were in radio contact with a directing center. The rapid evacuation by airplane had a splendid psychological effect on the wounded.

The medical officer at the clearing station has another difficult problem to decide as many men with minor injuries and feigned illness will drift back to this station. A dressing, a hot drink or stimulant, and a short rest will straighten out this patient and then he must be sent to join his fighting companions. The surgeon must be firm and decide as battles are not won by evacuated soldiers.

The evacuation hospital is equipped for all types of emergency surgery and staffed with operating teams assigned to regional surgery, as thoracic, abdominal, cranial and neural orthopedic, genito-urinary and plastic maxillofacial. All the usual anesthetics can be supplied at this hospital. During and after a battle relieving teams, working night and day care for a large number of wounded. These hospitals are located at a railroad or on a waterway and evacuate the sick and wounded as soon as patients can be safely moved to the fixed base and general hospitals in the zone of the interior.

An interesting report from England in the treatment of wounds of the extremities is that the wounded extremity is carefully debrided, sprinkled with sulfanilamide crystals, bandaged and the extremity put in a plaster cast. The patient is evacuated and the cast is not disturbed so long as the patient's condition is satisfactory. The results so far reported are excellent. This treatment should be instituted at the evacuation hospital.

One of the newer developments of the medical department is the trailer hospital which was constructed under the supervision of Colonel Garfield McKinney, MC at the Field Service Laboratory at Carlisle Barracks, Carlisle, Pennsylvania and at the request of Colonel McKinney the surgical staff at the Walter Reed General Hospital and I planned the equipment.

The trailer operating room (Fig. 1) has floor space 11½ by 7½ feet storage space, the forward part for instruments, anesthetics, drugs, etc. a scrubbing sink, an instrument sterilizer, ample ceiling light facilities, double plate glass windows each side, walls and ceilings insulated with 2 inches of cork, zero heating and cooling equipment, and a 100 gallon water tank in the forward part.

In supplying the instruments, the various specialists at the hospital were asked to select necessary instruments and omit unnecessary types. We selected a basic set with which most general surgical operations can be done. Then we selected supplemental sets to cover the regional operations. The supplemental sets are abdominal, thoracic, ear, nose and throat, eye, orthopedic, genito-urinary, a scope and cranial and brain. There are basic sets and 1 each of the supplemental sets with each trailer operating room. These sets, basic and supplemental sets will be furnished to all Army hospitals. At the base and general hospitals, power driven instruments for orthopedic and skull cases will be furnished to supplement the basic sets and, of course, types of anesthetics will be available.

The anesthetics for the trailer operating room are the less bulky types: inhalant ether, spinal, novocain, nupercaine, spinal, cocaine and pontocaine, local infiltrating procaine, cocaine for eye conditions, rectal, avertin. The Heidbrink Gas Machine Company, working with Captain William Nichol of the Medical Corps, has developed a small compact gas machine to supplement avertin and spinal anesthetics. Due to the rather small space, a large machine and tank will be in the way and there is some doubt to the feasibility of a continuous supply of gas tanks. It is estimated that with 3 operating teams, 20 major operations can be done 24 hours in each trailer operating room. The trailer operating room will be accompanied by a sterilizer trailer, a kitchen trailer and power plant for electric current.

During use the trailer operating room is backed up to an opening in a receiving tent. When all the casualties have been operated upon the trailers can move on to other fields, while doctors and nurses sent

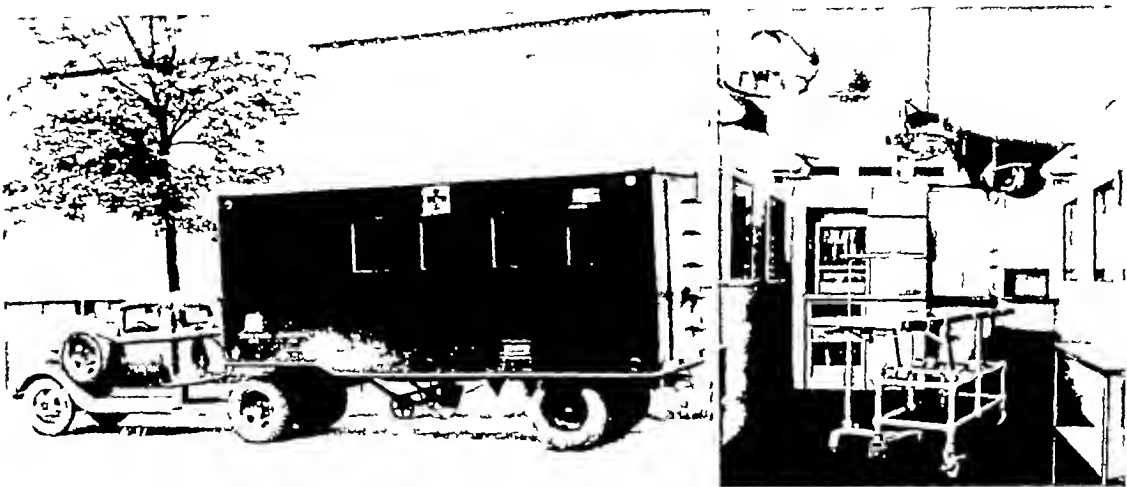


Fig 1 Ambulance unit with interior view (Reproduced through courtesy of Army Medical Museum)

from the rear take over the now immobilized hospital, and the mobile units proceed to other localities

At the Army Medical Center in Washington, D C, we have a professional service school where all recently commissioned medical officers are sent for a 4 months' course of training in the principles of sanitation and preventative medicine, bacteriology and laboratory methods, and clinical instruction in orthopedic surgery. On completion of this course they are sent to the Medical Field Service School at Carlisle Barracks, Pennsylvania, where they receive 5 months' training in field work, practical sanitation, removal of wounded from the field, proper methods of preparation of patients for litter and ambulance transportation, and instruction in the handling of field hospitals and ambulance companies. On completion of this course they are ordered to various posts and general hospitals and have an opportunity to put to practical use the knowledge gained.

These young medical officers come from all parts of the United States, are graduates of reputable medical schools, and have interned in the best hospitals of the country, a fixed number each year apply for an internship in some of our general and large station hospitals of the Army. Each man accepted is recommended by the dean of his college and reports to the specified hospital on June 30. The

internship, when completed, gives him the necessary credits for his graduation. During their internships these young doctors receive board, room, and 60 dollars a month. At the completion of their internships and if recommended by the Medical Board, they are offered a commission as First Lieutenant in the Medical Corps of the Army. We secure many fine medical officers in this manner.

The Surgeon General, from time to time as vacancies occur or an increased quota of medical officers is authorized, announces dates for examination for commission in the Medical Corps. Examinations are held at various Army posts throughout the United States. Our physical examinations are very exacting as we hope each officer accepted will be physically qualified for at least 30 years' service.

During recent meetings in Washington, D C, under the direction of the National Board of Research and the Surgeon Generals of the Army, Navy, and Public Health Service, well known physicians and surgeons called from all parts of the United States have started an intensive study of the better methods of treating battle casualties and handling respiratory and other infectious diseases. Dr Evarts A. Graham is the chairman of the general committee and each member of the general committee is the chairman of a subcommittee for study of the

various types of regional surgery anesthesia, chemotherapy etc. Each committee is getting together in manuals all data covering the best method of treating the region wounded, and in the event of war these manuals will be published in a concise form to outline the better procedures, so that a young surgeon may quickly review and follow them.

An example in the plastic maxillofacial manual would be *don't remove loosely attached bone fragments*. Support jaw with bandage and put an airway through the mouth. *Don't remove lacerated skin or muscles*. Save it for the plastic surgical team at the evacua-

tion or fixed hospitals. Other manuals will give similar types of information. It is desirable that these manuals be of pocket size and on one page the *do's* and *don't's* summarized.

In conclusion may I say that if any of my statements help the junior medical officer in finding his place in the Army I shall feel well repaid.

#### REFERENCES

1. SHELLEY, SAM F. EMERY, HIRSH E. and MA V. I. R. C. Comparative studies on traumatic shock under ether and sodium amytal anesthesia. *Ann Surg* 95, 94-111.
2. Translation of German Experiences in Poland Army Medical Bulletin N 33

# THE NATIONAL RESEARCH COUNCIL COMMITTEE ON SURGERY

## A Brief Statement of Its Work

LEWIS A. GRAHAM, M.D., F.A.C.S., St. Louis, Missouri

ANYONE who recalls the confusion and the hysterical haste which were conspicuous features of the medical preparations of the last war will doubtless be relieved to learn that if war comes this time there will be a minimum of confusion. At the time of the last war practically no medical preparations were made until after we were actually engaged in the conflict. Now, however, active steps are being taken to prepare adequately the medical corps of the Army and Navy well beforehand.

To accomplish this preparation there has been a division of labor, and different tasks have been assigned to different organizations. I shall speak briefly of the National Research Council Committee on Surgery. First a few words about the National Research Council. In 1916, realizing that this country was likely to be drawn into the maelstrom of the European war, President Wilson organized the National Research Council to give to the Government such advice on scientific matters of various kinds as might be needed in a national emergency. Since the war the existence of the Council has been maintained. It consists of several divisions, of which one is that of the medical sciences, and it shares with the National Academy of Science the beautiful building at 21st Street and Constitution Avenue, Washington.

In May of this year, realizing that again the nation was confronted with the possible danger of war, the Surgeons General of the Army, the Navy, and the Public Health Service called upon the National Research Council for advice regarding the newer ideas on the prevention and treatment of shock and on the applicability of the newer chemotherapeutic drugs to war infections. The chairman of the Division of Medical Sciences, Dr. Lewis H. Weed, accordingly appointed some committees to investigate the particular problems. It was soon realized, however, that the advisory work should have a much wider scope than that upon which the original work was undertaken. At the present time, in addition to

the two original committees on shock and on chemotherapy, respectively, there are three other major committees—one on surgery, one on medicine, and one on information. Of these major committees there are thirty subcommittees at work. The selection of the committees has been made after consultation with various civilian individuals and groups as well as with officials of the Army, Navy, and Public Health Service.

In order that there should be as little overlapping of function as possible the National Research Council's committees limit their activities to such fields as experimental research on problems that come up, matters of all kinds which concern the professional activities of the reserve medical officers personnel, advice on medical equipment and instruments, and in short anything with which the doctor as a medical officer is likely to be involved, aside from purely military or naval activities. As you know, the huge task of cataloging and classifying the medical profession of the country has been taken over by the American Medical Association. No other agency is so well equipped to carry out this function. We are fortunate that in this country at this time of peril to the nation there exists so efficient and powerful an organization able to perform this gigantic task of supplying to the armed forces of our country a list of experts available for every conceivable kind of medical work. The National Research Council Committee on Surgery is co-operating with the American Medical Association Committee to facilitate this work as much as possible. As a result of the careful evaluation and appraisal of each doctor's abilities, it is expected that there will be far fewer round pegs in square holes than in the last war. There will be no opportunity for any doctor, merely on the basis of wishful thinking, to be recognized by the army as a specialist. The committees which will scrutinize his record and assign him accordingly to his proper place will be guided only by his training and performance. Recently another much needed committee has been organized of which our own Dr. Abell is chairman. It has been recognized for several months that a committee to deal with all

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those affairs which will concern the health and medical activities of the civilian population in case of war should be organized as a part of the Council of National Defense, and recently President Roosevelt has appointed such a committee. Dr. Abell himself will tell you more of this committee. I may say however in order to emphasize the harmony and co-operation with which the various medical preparedness committees are working that Dr. Abell besides being chairman of this last mentioned committee is also chairman of the American Medical Association committee and a member of the National Research Council Committee on Surgery.

As examples of the sort of work that is being done by the National Research Council Committee on Surgery besides what has already been mentioned, it may be said that an extensive program of research on surgical infections is about to begin. Various pocket manuals of instruction of how to deal with different kinds of wounds are being prepared. Consideration is being given to the use of more protective armor than the steel

helmet. The most suitable methods of anesthesia for different kinds of operations and for use in different kinds of hospitals, together with the various types of anesthesia apparatus, are being discussed. Similar considerations are being given to the use of the x-ray under the varying conditions of warfare. Many research projects are being given consideration, some of which will probably be set in motion soon. These are only some of the activities of that committee. We are not concerned with the granting of commissions in the reserve corps to any individuals except through our co-operation with the American Medical Association in the evaluation of the qualifications of individual specialists. We have however expressed the hope that the course of training of the young surgeons will not be seriously interrupted and that the work of the civilian hospitals will not be crippled by a wholesale removal of the house-staffs for military purposes. There is good reason to think that this hope which is shared by all who have an intelligent appreciation of the needs of the hospitals will be realized.

## TWENTY-THIRD ANNUAL HOSPITAL STANDARDIZATION CONFERENCE

MALCOLM T. MACEachern, M.D., Chicago, Illinois

HOSPITAL Standardization is an exceedingly involved activity which nevertheless it is possible to crystallize in a single expression of its progress every year—the “Approved List.” The announcement of the list of 2,806 approved hospitals at the twenty-third annual Hospital Standardization Conference, held in Chicago in October, 1940, and its publication in the approval number of the *College Bulletin*, may seem to the uninformed observer to have been routine procedures, which have lost their stimulating effect because of the many regular repetitions. Instead, issuance of the list seems to acquire added significance each year, to judge by the repercussions that follow from the borderline hospitals which expected to be included but were not, and by the inquiries about how to meet the requirements some of which come from hospitals which were scarcely considered even as aspiring to approval.

Some things there are upon which steady hammering away with expression of ideals and the citing of examples creates an interest more substantial than that which is won by novelty. Hospital Standardization has earned a place in this category. Its influence has been cumulative. While it is true that a great many hospitals occupy an assured position on the approved list, that a doubt never arises about finding their names on it year after year, nevertheless even upon them the activity has a constantly stimulating effect because the fact of reconsideration for approval each year makes it necessary for them consciously to keep abreast of improvements in all phases of hospital work. Every year it becomes an unpleasant necessity to omit from the list some hospital from which protest is made on the sole ground that it has been approved for 10 or 15 years, and its facilities and methods are as good as they were when approval was granted. The answer to that protest is that the interpretation of the Minimum Standard is progressive from year to year, and that in the march of progress the hospital that is static falls farther and farther to the rear until finally it is behind the vanguard of approved hospitals and deserves no place in their ranks. Though a hospital has been twenty times approved, it has no assurance that it will be

approved the twenty-first year unless it is positive that in every respect it is up-to-date as of the current period in the advance of hospitals.

Of course, a great satisfaction in hospital standardization work is the handful of hospitals that are each year converted from the borderline condition to full acceptance of the standard. The satisfaction does not lie in being able to show an increase in the number of approved hospitals, but in making available to more patients the benefits of hospital service that is properly organized, controlled, and directed. Whenever a hospital is added to the approved list, the correct way to evaluate the gain is by the additional number of patients who are as a consequence receiving better care. Patients in the smaller hospitals and in hospitals in areas distant from the medical centers are especially in need of the assurance that they are receiving a high quality of care, and this assurance the approved hospital is entitled to give.

So far as the smaller town is concerned, Hospital Standardization has been a timely activity, coincident with a rapid general trend toward better distribution of the comforts, conveniences, safeguards, and luxuries of life. In a recent article in *Harper's Magazine* by Bernard De Voto on “Main Street Twenty Years After,” an excellent description is given of the way in which standardization has transformed the average town. Retail stores, schools, transportation and communication systems, power and light facilities, and sanitary precautions, have been immeasurably improved through standardization even in small villages. Hospital service should have kept pace with this advance, and it is the aim of Hospital Standardization that at least the same favorable comparison with facilities in the large cities be attained by the hospitals as by other public services in the smaller communities. Not all of the unapproved hospitals are by any means in the less populous areas, it is true, but so large a proportion of them are that the need there should be emphasized. De Voto says that standardization, “which so enraged the intellectuals of the 1920's, has in reality annihilated much that was deadening and disruptive in rural existence.” To which should be added that it has also annihilated

much that was distressing and dangerous, when sickness or accident struck, by making it possible for a hospital to give good service even when its capacity is as few as 5 beds.

Hospital Standardization is not only always reaching out to influence for good the below grade hospital but it is also working for better service to the individual patient in the approved hospitals. A hospital that readily meets the general standards for approval, may yet be ministering poorly to the needs of certain types of patients. These needs are discovered in the surveys and through contacts with hospital personnel who are aware of them and are brought up for discussion at the Hospital Standardization Conferences in connection with the Clinical Congress and sectional meetings of the College. An example was the conference on convalescent care at the Clinical Congress in October in which the needs of a number of different types of convalescent patients were discussed by specialists in each field. The keynote was set by the title of the address of the presiding officer Dr. Harry E. Mock, of Chicago, "Convalescent Care—the Missing Link in the Care of Many Patients." The special needs of the surgical, the medical, the cancer, the fracture, the orthopedic, and the pediatric patient were presented, respectively by Dr. Donald B. Wells, of Hartford; Dr. Newell C. Gilbert, of Chicago; Dr. Frank E. Adair, of New York; Dr. Robert H. Kennedy, of New York; Dr. Frederick C. Kidner, of Detroit; and Dr. Louis A. Schwartz, of Detroit. Dr. Gilbert made a particularly salient point when he departed from the idea of "convalescence" toward that of using the convalescent home partly as a "preventorium," urging that hospitalization could frequently be avoided, with great economic saving, by preventive care in this type of institution. Dr. William H. Walsh, of Chicago, in describing the essentials in planning of institutions for convalescent care, said that surveys have shown that an average of 12 per cent of patients occupying beds for acute illness in hospitals are suitable cases for convalescent care, and remarked that "if and when adequate

convalescent facilities are made available, there will be a considerable reduction in the number of chronic cases to be provided for." Elizabeth G. Gardner, of New York, in a talk on "Socio-Economic Aspects of Convalescent Care," urged the increased consideration of proper convalescent care as a means of more speedily returning the patient to his or her usual function as worker or housewife. E. H. L. Corwin, Ph.D. of New York, in discussing "Minimum Standards for Convalescent Hospitals," suggested that "with the oncoming national emergency it may be of great moment to be able to transfer to convalescent homes, hospital patients who have passed the acute stage of their illness or disability" and he therefore urged that the American College of Surgeons "duplicate the splendid work it has done in the hospital field by developing minimum standards for convalescent hospitals and supervising their adoption," saying that, after all, "the medical and surgical job is not completed upon the patient's discharge from the hospital."

It may well be that the needs of the national defense program as it concerns hospitals will indicate the desirability of more attention to the needs of the convalescent patient, and will act as a spur to greater development of facilities to serve him. The *Minimum Standard for Hospitals* is sufficiently elastic to provide a gauge of approval for the convalescent institution, and if after further study and investigation it seems desirable to formulate as a guide a special auxiliary minimum standard, this can readily be done as it was in the case of cancer clinics and of plans for graduate training in surgery in hospitals.

The Hospital Standardization conferences are valuable in bringing new needs to the surface and in enabling exchange of views with hospital personnel on current problems. They together with the personal surveys on which the approved list is based, keep Hospital Standardization close to the ground, broadening its scope to embrace developing needs, and making approval a practical, attainable goal for any hospital and a direct influence for better service to every patient.

# THE 1940 CLINICAL CONGRESS

JOHN A WOLFER, M D , F A C S , Chicago, Illinois

SOME dominant note in response to a scientific development or a social need seems to ring through each Clinical Congress, and, as might have been expected, the 1940 Congress was tuned to the current interest in national defense. Though in only one session were the discussions predominantly centered upon the physician's rôle in military preparedness, nevertheless the additional incentive for research and experimentation, which preparedness gives, kept rising to the surface in the talks and comments at many of the meetings. A report on the work and plans of the committee on surgery of the National Research Council was presented by its chairman, Dr. Evarts A. Graham, the new president of the American College of Surgeons, and the aims of the health and medical committee of the Council of American Defense to co-ordinate the efforts of all agencies working for medical preparedness were described by its chairman, Dr. Irvin Abell, chairman of the Board of Regents, at the Wednesday evening session. Representing the medical corps of the United States Army, Brigadier General Raymond F. Metcalfe told of the correct attitude of medical officers toward draftees, and described some of the applications in military service of new developments in medicine.

The Surgeon General of the United States Navy, Rear Admiral Ross T. McIntire, brought to the attention of the public the plans for "Medical Preparedness for National Defense" in an address sponsored by the College over the National Broadcasting Company network on Sunday evening preceding the opening of the Clinical Congress. Introduced by Dr. Abell, Admiral McIntire said in part:

"It is extremely gratifying to find the splendid co-operation that is being given to the Army and the Navy by such organizations as the American College of Surgeons. The work of the College in the industrial field of medicine is playing a most important part in plans for expansion in that field. The Army and the Navy will demand a great deal from the medical profession, the nurses, the hospitals, and all other allied organizations that have to do with health. We in the military services are being exceedingly careful not to rob our industrial centers, our small towns, and rural communities of proper medical and hospital care.

"This is being done by the preparation of a broad and comprehensive plan by which proper selection of personnel will be made in a rational manner."

Chairman of the Committee on Arrangements

Brigadier General Metcalfe gave a talk over the Columbia Broadcasting System network on Thursday evening of the Congress in which, following an introduction by Dr. Graham, he told of a preparedness program, "not for war, but to prevent war," and assured the mothers of America that their sons, if called to military service, will receive "good food, warm clothing, healthful training, instruction in a particular branch of service, instruction in personal hygiene, and the best of medical care if sick or injured."

Particular mention is made of these broadcasts because of the omission from the 1940 Clinical Congress program of the heretofore customary community health meeting, and because the chairman of the arrangements committee is also chairman of the Committee on Public Relations and hence is immediately concerned with those aspects of the Congress which are of interest to the public as well as those that appeal to the profession. Through the co-operation of the public service divisions of the large broadcasting systems it was possible to convey to the public the timely messages of the Surgeon General of the Navy and the assistant to the Surgeon General of the Army.

The 1940 Presidential Meeting or Convocation was lacking, of necessity, in one feature to which we have become accustomed, the introduction of foreign guests, but in other respects was characterized by the usual impressiveness. The class of initiates received into fellowship was exceptionally large—there was a total of 611 new members—which brings the enrollment of the Fellows to well over 13,000.

The clinics in some forty of the approved hospitals in the Chicago area were exceptionally well attended, and again it was demonstrated how helpful it is to the individual surgeon to have the program so arranged that one who is interested in a specialty can if he wishes give almost undivided time to its study in the clinics and in the scientific sessions, panel discussions, and group clinical conferences. The clinical conferences were a new feature in 1940, and a popular one, with overflow attendance registered in many instances. The ophthalmologists and otorhinolaryngologists, in particular, expressed great satisfaction with the six conferences arranged for them on three successive mornings.

The symposium on cancer attracted the usual wide interest, and considered in conjunction with the announcement of the list of 345 approved cancer clinics in hospitals in the United States and Canada, and of additions to the archives of 5 year cancer cures which bring the total to 36,078 constituted one of the most important events of the Congress, indicating the concentrated effort that is being directed toward gaining better control of this disease.

Another outstanding session was the symposium on fractures and other traumas. This session, also, should be evaluated against its background of intensive activity by the College, especially in connection with the treatment of fractures which has been improved largely through the efforts of the Committee on Fractures and the Regional Fracture Committees which the chairman of this meeting announced, now number 85 and have a total membership of 1,400.

The reports of the Committee on Cancer and of the Committee on Fractures and Other Traumas were presented in detail at the annual meeting of the Fellows on Thursday afternoon, together with reports of the Library and Department of Literary Research, the Department of Hospital Standardization, the Department of Clinical Research and others, giving an impressive picture to the Fellows of the great amount of activity bearing directly upon improvement of medical and hospital service in which the College is engaged.

As to new developments reported at the Congress, that in which there is probably the widest interest was the increasing use of the sul-

fonamides: one speaker told of the use of these compounds as aids to surgery and another described the rapid healing of wounds received in war or accidents when sulfanilamide was applied. Another interesting report was that the acute symptoms of Ménière's disease may be relieved by injections of histamine. The permanent cure of Ménière's disease by dividing the auditory nerve was reported in 401 operations, with only 1 death which was due to meningitis. The use of the anti-blood-clotting substance, heparin, in the successful grafting of pieces of veins to bridge gaps in wound-torn arteries was announced. The results of high voltage radiation therapy in gynecological cancer were reported.

The 940 Congress brought forth many new ideas in applying the scientific developments in practice in hospitals. The concurrent holding of hospital conferences serves to emphasize the important place of surgery in the hospital and the desirability of its strict control. It serves also to keep before the surgeon's mind the many services in the hospital, proper performance of which contributes to more successful surgery.

The surgeons of Chicago are proud to have been hosts to the thirtieth Clinical Congress, as they were to the first, held in 1910. Eight times our city has been the setting for this illustrious gathering. The medical schools and hospitals of Chicago co-operated generously in arrangements for the 1940 meeting, and the committee gratefully acknowledges their support and that of the individual speakers, leaders of discussion and collaborators, exhibitors, and all who in any way helped toward the success of the Congress.

# FUTURE NEEDS FOR GRADUATE TRAINING IN GENERAL SURGERY AND THE SURGICAL SPECIALTIES

DALLAS B. PHÉMISTER, M.D., F.A.C.S., Chicago, Illinois

IN its program of graduate training in surgery the American College of Surgeons has proceeded on the theory that all hospitals, be they large or small, situated in metropolitan centers or in the smaller towns, are educational institutions in the truest sense when they follow the principles of hospital standardization. The medical school lays the foundation for the education of the physician, but the hospital erects upon that foundation the framework of practical training. In proportion as the educational rôle of the hospital is conscientiously planned and played, the physicians and surgeons who enter practice will be competent and trustworthy.

The medical schools alone, important and fundamental as their place is, can never produce surgeons sufficiently qualified to be entrusted with people's lives. Apprenticeship to an older practitioner is now less and less frequently employed as a method of training. Hence in our day the hospital, every hospital, must definitely assume its due share of teaching responsibility if the public are to be given the full advantages of progress in medical science. This is a never ending responsibility, not only in respect to the year by year entrance and outgoing of internes and residents, but in its application to the progressive education of every member of the staff. Even the hospital that has no internes or residents may so organize its staff that there is effective control by the more experienced members over those not so well qualified, and this is an educational function.

What the College hopes to do, and what it has already in some degree accomplished, is to lighten the consciousness of hospitals to their educational obligations and opportunities. The graduate training program is simply hospital standardization carried forward in one of its educational phases. Rather conspicuous proof of success in arousing a consciousness of educational responsibility was furnished by the publication in the October, 1940, *Bulletin*, of detailed descriptions of the plans for graduate training in general surgery and the surgical specialties of two hundred hospitals in the United States and Canada which have been approved for this purpose. Many hospitals have initiated graduate training pro-

grams, and others have amplified and revised theirs, as a result of encouragement by the College, and guidance which in the past year has taken tangible form in a published *Manual*, available now in reprint form under the same cover with the descriptions of the approved plans.

The growth in the number of hospitals participating in approved plans from 179 on October 1, 1939, to 200 on October 1, 1940, together with the increase in the number of men in training in general surgery and the surgical specialties from 1,606 in 1939 to 1,745 in 1940, shows the widening interest. There is also indicated a definite trend toward development of plans of graduate training of three or more years' duration in general surgery, as well as in many of the surgical specialties, that is significant. Of those completing work in general surgery in 1940, 73 per cent received three or more years' training.

A number of the hospitals whose plans for graduate training in surgery have been approved are a part of universities and medical schools. Valuable as such direct connections are in facilitating study of the basic sciences, a lack of them and also of sufficient and varied clinical material can be surmounted by affiliation with some medical school and by co-operation with other hospitals. So thoroughly convinced is the College by its experience with this program that the standards of surgical performance in a hospital are almost automatically raised when it undertakes to provide graduate training in surgery, that the theory upon which future work will be based is that reasonably wide participation is eminently desirable, and encouragement and help will continue to be given the hospital which establishes affiliations in order to furnish a well rounded program.

Better distribution of thoroughly qualified surgeons is the great need, and an obvious way of helping to effect this is to have surgical training centers more widely distributed. Some of those who complete their training in districts away from the leading medical centers will remain there to practice, and not only the institutions definitely organized for teaching but others in the vicinity as well, will benefit ultimately by having better surgeons on their staffs. The cycle of benefits will

Chairman of the Committee on Graduate Training for Surgery

be advanced by the attraction of surgeons trained in the medical centers, to the improved hospitals in the less populous areas.

It is a long view that the College is taking in the graduate training program—a view that yields no prospect of a goal possible of complete attainment. To the argument that enough surgeons are being trained now to fill the need in numerical terms, the conclusive answer is that not all of these surgeons are being trained well enough, nor are there likely to be too many well trained surgeons, at least in the generations immediately ahead of us. For medical schools a curriculum can be established, adherence to which forms the basis of approval for hospitals so many intangible factors are involved in addition to provisions for basic science study and supervision, that constant and continuous work with them is essential to progress. This is especially true in view of the fact that, after all, the teaching function is subordinate to the chief purpose of serving the patient and is worthy of promotion only because

when properly carried out, it contributes to improvement in that primary aim.

The program is an integral part of the purpose of the College to elevate the standards of surgery. It is notable for interpreting that purpose to mean that the standards should be elevated everywhere. Because the need for better surgery is greatest in that type of institution the keenest satisfaction is felt when the heretofore "non-teaching" hospital assumes teaching and training responsibilities and meets the requirements for approval. The College has closely at heart the welfare of patients in all types and sizes of hospitals and is constant in striving for higher standards of training for surgeons and better control of surgery.

Hospital standardization and graduate training for surgery as well as for all other branches of medicine, should progress hand in hand. A hospital of the requisite bed capacity should be recognized as possessing adequate standards which does not also conduct a program for adequate training for surgery.

# CHICAGO COMMITTEE ON ARRANGEMENTS

## EXECUTIVE COMMITTEE

John A. Wolfer	Warren H. Cole
Chairman	Vernon C. David
Charles B. Puestow	Marshall Davison
Secretary	Harry S. Gradle
Fred L. Adair	Michael L. Mason
William E. Adams	Oscar L. Nadeau
William J. Baker	Eric Oldberg
Frederic A. Besley	Samuel Salinger
Alexander Brunschwig	Charles F. Sawyer
Fremont A. Chandler	Kellogg Speed

## HOSPITAL REPRESENTATIVES

Alexian Brothers—George L. Apfelmach  
 Augustana—Oscar E. Nadeau  
 Albert Merritt Billings and Bobs Roberts Memorial—  
 Dallas B. Phemister  
 Chicago Lying In—Fred L. Adair  
 Chicago Memorial—Peter S. Clark  
 Children's Memorial—Albert H. Montgomery  
 Columbus—Daniel A. Orth  
 Cook County—Marshall Davison  
 Evangelical—G. Henry Mundt  
 Evanston—Frederick Christopher  
 Grant—A. G. Zimmerman  
 Hearst—John A. Graham

Holy Cross—John T. Ruzic  
 Illinois Eye and Ear Infirmary—Thomas D. Allen  
 Illinois Masonic—Walter C. Bornemeier  
 Jackson Park—Arrie Bamberger  
 Loretto—James A. Valentine  
 Mercy—Charles T. Sawyer  
 Michael Reese—Ralph B. Bettman  
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 Mount Sinai—Jacob M. Mora  
 Municipal Tuberculosis Sanitarium—Richard Davison  
 Norwegian American—Harold A. Sofield  
 Passavant Memorial—Loyal Davis  
 Presbyterian—Vernon C. David  
 Ravenswood—Darwin B. Pond  
 Research and Educational—Warren H. Cole  
 St. Anne's—George T. Thompson  
 St. Anthony de Padua—Frederick W. Slobe  
 St. Bernard's—John G. Frost  
 St. Elizabeth's—Martin G. Luken  
 St. Joseph—Hugh McKenna  
 St. Luke's—Selim W. McArthur  
 St. Mary of Nazareth—George M. Mueller  
 Shriners' for Crippled Children—Beveridge H. Moore  
 Swedish Covenant—Karl L. Vehe  
 Veterans Administration—Paul F. Brown  
 Washington Boulevard—Arthur R. Metz  
 Wesley Memorial—Raymond W. McNealy  
 Women and Children's—Maude H. Winnett

The Thirty-first Annual Clinical Congress of  
 the American College of Surgeons will be held  
 in Boston November 3-7, 1941



# CLINICAL CONGRESS TECHNICAL EXHIBITION

**L**EADING manufacturers of and dealers in surgical instruments, hospital apparatus and supplies, diagnostic and therapeutic apparatus, pharmaceuticals, and publishers of medical and surgical books were represented in the Technical Exhibition at the Stevens Hotel in Chicago, October 21-25 1940.

W. D. Allison Co. Indianapolis  
A. S. Aloe Co. St. Louis  
American Cystoscope Makers, Inc., New York  
American Hospital Supply Corp. Chicago  
American Journal of Surgery New York  
American Safety Razor Corp. Brooklyn  
American Sterilizer Co., Erie, Pa.  
D. Appleton-Century Co. New York  
Armour & Co. Chicago  
Austral Laboratories, New York  
Assoc's National Physicians Exchange Chicago  
C. R. Bard, Inc., New York  
Bard Parker Co. Dursbury Conn.  
W. A. Baum Co., Inc., New York  
Baxter Laboratories, Glenview, Ill.  
Beckton, Dickinson & Co. Rutherford, N. J.  
Bell & Howell, Chicago  
Johns Berbeck & Sons, New York  
Blitcher Corp. Los Angeles  
Blackstone Co., Philadelphia  
Burdick Corp., Milton, Wis.  
Burros Co., Chicago  
S. H. Camp & Co. Jackson, Mich.  
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Gilbert Hyde Chick Co., Berkeley, Calif.  
Cliffhold Co. Marshalltown, Iowa  
Clay Adams Co. New York  
Warren E. Collins, Inc. Boston  
Comper Manufacturing Co., Pittsfield, Mass.  
Conformal Footwear Co. St. Louis  
Crane Co., Chicago  
Crescent Surgical Sales Co., New York  
Cutter Laboratories, Berkeley, Calif.  
R. B. Davis Sales Co. Hoboken, N. J.  
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J. A. Deknatel & Son, Queens Village, N. Y.  
DePuy Manufacturing Co., Warsaw, Ind.  
A. W. Dick, Detroit  
Duke Laboratories, Stamford, Conn.  
Eastman Kodak Co., Rochester, N. Y.  
E. & J. Co. of Pennsylvania, Philadelphia  
J. H. Emerson Co. Cambridge, Mass.  
Furniture Center Co., Evansville, Ind.  
Foregger Co., New York  
General Electric X-Ray Corp. Chicago  
Gordbrod Bros. Silk Co., Philadelphia  
Hamilton Manufacturing Co. T. Rivers, Wis.

Hanovia Chemical & Manufacturing Co. Newark, N. J.  
Paul H. Hoeber, Inc. New York  
Hospital Liquids, Inc., New York  
Johnson & Johnson, New Brunswick, N. J.  
Jones Metabolism Equipment Co. Chicago  
Kennedy Webster Electric Co. Chicago  
Les & Frager Philadelphia  
Lewis Manufacturing Co. Walpole, Mass.  
Liebel Flaming Co. Cincinnati  
Eli Lilly & Co. Indianapolis  
J. B. Lippincott Co. Philadelphia  
MacGregor Instrument Co. Boston  
Majestic Surgical Instrument Co. Chicago  
Mamilton Rubber Co. Mansfield, Ohio  
McKesson Appliance Co. Toledo  
Medical Bureau, Chicago  
March & Co. Raba, N. Y.  
C. V. Mosby Co., St. Louis  
V. Mueller & Co. Chicago  
New York Medical Exchange, New York  
Ohio Chemical & Manufacturing Co. Cleveland  
Oxford University Press, New York  
Oxygen Equipment & Service Co. Chicago  
Petrolog Laboratories, Chicago  
Physicians' Record Co., Chicago  
Parker X-Ray Corp. New York  
W. F. Price Co. Hagerstown, Md.  
Promethes Electric Corp., New York  
Pumila Compressed Gas Co., Kansas City, Mo.  
Radford Chemical Co., Inc., New York  
Radford Foundation Corp., New York  
Richards Manufacturing Co. Memphis, Tenn.  
Ritter Equipment Co., Rochester, N. Y.  
Safety Gas Machine Co. Chicago  
Sanborn Co., Cambridge, Mass.  
W. B. Saunders Co. Philadelphia  
Scudder-Morris Co. Madison, Wis.  
Schering Corp. Bloomfield, N. J.  
Schering & Glaxo, New York  
J. R. Seabrandt Manufacturing Co., Kansas City, Mo.  
J. Siler Manufacturing Co. Long Island City, N. Y.  
Smith, Kline & French Laboratories, Philadelphia  
Smith & Nephew, New York  
C. M. Sorenson Co., Long Island City, N. Y.  
E. K. Squibb & Sons, New York  
Stora Instrument Co. St. Louis  
Surgery, Gynecology and Obstetrics, Chicago  
Taylor Instrument Co. Rochester, N. Y.  
Charles C. Thomas, Springfield, Ill.  
Tow & Co., Seattle, Wash.  
Wall Chemical Corp. Detroit  
Wallace & Therman Products, Bellevue, N. J.  
Williams & Williams Co. Baltimore  
Wilson Rubber Co., Canton, Ohio  
Windthrop Chemical Co. New York  
Max Woehner & Son Co. Cincinnati  
Zimmer Manufacturing Co. Warsaw, Ind.

HENRY CLUTTERBUCK (1767-1856) Surgeon and physician, courageous defender of medical ethics, the most effective lecturer on materia medica and the practice of physic in London, author of "Inquiry into the Seat and Nature of Fever," 1809



# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### CRANIOCEREBRAL INJURY

ALFRED P. ROWLAND, M.D., F.A.C.S., and DAVID O. WEINER, M.D., St. Louis, Missouri

**D**URING the period of 1934 to 1937 inclusive, there were 634 cases of severe craniocerebral injury and 604 cases of concussion admitted to the St. Louis City Hospital. All deaths were included under the heading of acute craniocerebral injury and the mortality of this group was 38.0 per cent. This checked closely with the last report from Bellevue Hospital of 37.8 per cent (12).

However, it compared quite unfavorably with reports of Fay, Mock, Swift, Munroe and others of mortality rates varying from 17 to 26 per cent. Although some feel that institutions receiving all the patients with severe trauma from the street accidents of a large city will naturally experience a higher mortality than will the private hospital, we could not help but feel that this discrepancy was too great.

At this hospital due largely to the influence of Sachs, spinal puncture was rarely used as a therapeutic measure and only infrequently as a diagnostic measure in cases of craniocerebral injury. Hypertonic sucrose and dextrose intravenously and magnesium sulphate retention enema were the two dehydrating measures which seem to have been usually used. Little cognizance had been paid to the limitation of fluid intake as advocated by Fay in the treatment of these cases (1).

The use of hypertonic solutions intravenously as dehydrating agents seems to be universally accepted, except by Dandy, who feels that both of these measures are contraindicated in these cases.

The limitation of fluid intake does not seem to be as popular as the use of spinal puncture and dehydrating agents, at least it does not receive the important position in the therapy accorded the two other measures.

Since the cases of intracranial injury were admitted to two distinct staff units it was felt that we were in a position to evaluate these procedures in the therapy of severe intracranial injury. One unit which we shall designate as Unit A was opposed to the use of lumbar punctures as a therapeutic measure and during the first year did not actually restrict the fluid intake. Although sucrose intravenously was used on both units its use on Unit A was restricted as compared with its use on Unit B.

The visiting surgeons of Unit B consulted and agreed to the study which we termed "active dehydration" following basically the ideas as expressed by Fay (4) comprising (1) lumbar punctures, (2) intravenous injections of 100 cc. of 50 per cent sucrose and (3) limitation of fluid intake.

Regarding (1) the difficulty of securing relief from the treatment of intracranial injury because of the fact that these patients are

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*Henry Clutterbuck*

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### CRANIOCEREBRAL INJURY

AVERY P. ROWLETTE, M.D., F.A.C.S., and DAVID O. WINNER, M.D., St. Louis, Missouri

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However, it compared quite unfavorably with reports of Fay, Mock, Swift, Munroe and others of mortality rates varying from 17 to 26 per cent. Although some feel that institutions receiving all the patients with severe trauma from the street accidents of a large city will naturally experience a higher mortality than will the private hospital, we could not help but feel that this discrepancy was too great.

At this hospital due largely to the influence of Sachs spinal puncture was rarely used as a therapeutic measure and only infrequently as a diagnostic measure in cases of craniocerebral injury. Hypertonic sucrose and dextrose intravenously and magnesium sulphate as retention enema were the two dehydrating measures which seem to have been usually used. Little emphasis had been paid to the limitation of fluid intake as advocated by Fay in the treatment of these cases.

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Since the cases of intracranial injury were admitted to two distinct staff units it was felt that we were in a position to evaluate these procedures in the therapy of severe intracranial injury. One unit which we shall designate as Unit A was opposed to the use of lumbar punctures as a therapeutic measure and during the first year did not actually restrict the fluid intake. Although sucrose intravenously was used on both units its use on Unit A as restricted is compared with its use on Unit B.

The visiting surgeons of Unit B consulted and agreed to the study which we termed active dehydration following basically the formula as expressed by Fay. At no point did lumbar punctures or intracranial injections of 100 cubic centimeters of 50 per cent sucrose and limitation of fluid intake.

Regarding fully the difficulty of obtaining the restriction of intake of intracranial fluids the treatment of intracranial injury because of the fact that the patient is not

routinely seen and early treatment instituted by the resident staff. It was felt imperative that rules of treatment and some sort of outline be set up for them to follow. Accordingly the following routine was established.

1. Unconscious patients were treated for shock if present. Lumbar punctures were not performed in the presence of shock. Intravenous sucrose was not considered contra-indicated in the presence of shock. It has been our impression that uncomplicated intracranial injury is not usually associated with profound shock. The usual treatment of shock was administered except for the use of morphine which was felt to be contra-indicated.

2. If shock was not present or had been relieved and the patient was unconscious, a lumbar puncture was performed. A water type of spinal manometer<sup>1</sup> was used to measure the cerebrospinal fluid pressure. Although we recognize that it is sometimes difficult to ascertain an accurate pressure, due to the straining of the patient, as a general rule we felt that reasonably accurate pressure readings were obtained. During the early months of this study if the pressure was markedly elevated, it was reduced to one-half of the original reading at the time of the first tap, and this procedure repeated every 4 hours until the pressure was brought to normal. After 3 months, experiencing no untoward results, we adopted the routine of immediately reducing the pressure to normal at the time of the original lumbar puncture. The house officers who performed the lumbar punctures were thoroughly warned of the potential dangers of the procedure in the presence of increased intracranial pressure and were very cautious to remove the cerebrospinal fluid *very slowly*.

3. If the cerebrospinal fluid was grossly bloody (not just turbid) the canal was slowly drained dry (i. e. fluid allowed to escape until no more spontaneously dropped from the needle) the amount of fluid being removed to accomplish this varied from 15 to 45 cubic centimeters.

4. During the first 3 months of the study if the patient remained unconscious, punctures were repeated every 4 hours. This period

was then lengthened to 6 hours, because we found that usually the pressure tended to stay level for about 4 to 5 hours if after each puncture 100 cubic centimeters of 50 per cent sucrose was slowly injected intravenously. Punctures were discontinued with the appearance of consciousness unless the fluid was grossly bloody in which case they were continued every 6 hours until the cerebrospinal fluid was grossly clear. Sucrose was ordinarily continued for one or two injections after the patient regained consciousness. If the patient remained unconscious longer than 48 hours, punctures were checked once daily to make certain the pressure remained normal, until the patient regained consciousness.

5. Fluid intake was limited to 1000 cubic centimeters whether by mouth or parenterally. If the patient was unable to take fluids by mouth, fluids were usually administered in the form of 5 per cent dextrose in Ringer's solution intravenously. If the patient remained unconscious longer than 48 hours, this was increased to 1500 or 2500 cubic centimeters per 24 hours.

The persistence of unconsciousness was the criterion used to gauge the necessity of continuation of the dehydration regimen. Lumbar punctures and intravenous sucrose were rarely necessary after the first 48 hours and fluid restriction could usually be lifted after the third day. If the patient developed a fever the fluid intake was increased and taps continued longer than the usual period.

Cases were divided into (1) acute cranio-cerebral injury and (2) concussion. All deaths occurring in the concussion group were included in the first group. All cases with demonstrable intracranial injury or skull fracture were included in this series regardless of how severe associated injury was present elsewhere in the body. All deaths which occurred (2 deaths) prior to admission to the hospital wards were excluded from this series.

In the first group we included (a) all cases with an obvious compound skull fracture or cases with positive x ray evidence of skull fracture (b) traumatic cases unconscious until death (c) cases presenting the general features of a basilar fracture, that is, ecchymotic orbital lids, aural bleeding, grossly

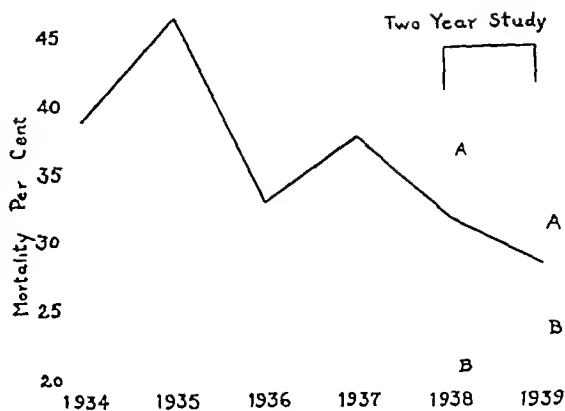
bloody spinal fluid, and (d) cases showing evidence of intracranial injury at autopsy

In the second group were included all cases ordinarily considered as concussions. Cases with a momentary or short loss of consciousness, following injury to the head, without symptoms of intracranial injury other than headache, nausea or vertigo, without grossly bloody spinal fluid and with negative x-ray evidence of a fracture of the skull were all included in this group. We feel that the inclusion of concussions in the statistics of some observers in the discussion of severe intracranial injury only clouds the issue and makes it impossible or difficult to compare results. We have made every effort to restrict cases in group 1 to severe injury, placing all cases, which were considered in group 2 until death, in group 1 in tabulating the results. Hence, we show no deaths under concussions. We had relatively more concussions than severe intracranial injury during the 2 year study period than we did during the 4 previous years.

#### ANALYSIS OF RESULTS

Of interest is a comparison of the etiological agents of this series and of one reported by Stewart from this hospital 20 years ago, in which he focused attention upon the tragic mortality attendant upon routine operative decompression in these cases. As predicted by Stewart, we have experienced a 25 per cent increase of severe craniocerebral injury almost entirely related to the automobile.

Because of the danger of herniation of the medulla and cerebellum into the foramen magnum resulting from spinal puncture in the presence of increased intracranial pressure, and because of the fact that in grossly bloody spinal fluids, we were draining the cerebrospinal canal dry and thus possibly inviting this complication, we were particularly on the watch for such findings at postmortem. Since in traumatic deaths, practically all victims are subjected to postmortem examination by the coroner, we were able to check our findings at autopsy in 88.8 per cent of the deaths of Unit A and 92.8 per cent of the cases of Unit B. In all deaths on Unit B in which spinal puncture had been used, postmortem examination was carried out in 100 per cent of these cases and



Graph 1 Total hospital mortality, severe craniocerebral injury

in no instance did we observe any evidence of medullary compression or "cone" formation. We feel that the constant use of the manometer and the *very slow* removal of fluid account for these results, because unquestionably this disaster may happen in intracranial injury (8), and we hazard an opinion that it may occur not only in cases with a block at the foramina of Magendie and Luschka, but in cases with a perfectly open system due to rapid removal of cerebrospinal fluid.

**Mortality experience** Graph 1 presents a summary of the total mortality experience for a 6 year period and the mortality of Units A and B during this study. During the year 1938-1939 in Unit A an excellent control series was available and it will be noted that the mortality on Unit B fell to 21 per cent which compared very favorably with the reports previously mentioned of mortality rates from 17 to 26 per cent. On Unit A, however, the mortality continued at approximately the average for the 4 year period preceding the study, that is, 37.3 per cent. During 1939-1940, due to a reorganization of the staff, the cases on Unit A were under different staff supervision, and approximately one-half of the cases had a limitation of fluid intake to 1500 cubic centimeters of fluid per day in addition to more widespread use of sucrose intravenously while the other half continued about as before. It will be noted that for this year the total hospital mortality fell to 28.5



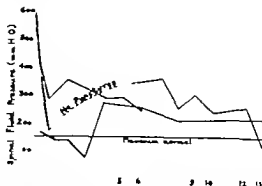


Graph 2. Rapid relief of cerebrospinal fluid pressure with spinal drainage.

per cent which was approximately 10 per cent less than the 4 year average mortality preceding the study or 38.9 per cent.

**Cerebrospinal fluid pressure.** Like Werdn we found that our patients tended to fall into two groups one (Graph 2) in which there was a progressive fall in cerebrospinal fluid pressure which constituted the usual response, and the other (Graph 3) in which the pressure continued high, despite repeated spinal drainage, dehydration, and limitation of fluid intake. It is of interest that our curves are similar Werdn apparently performing daily spinal drainage while we followed the same practice every 6 hours. In our cases the cerebrospinal fluid pressures generally reached normal limits in 48 hours, while he shows a like result in his graphs accomplished in usually 4 to 6 days. As has been noted by many observers, we found no consistent correlation between the clinical condition of the patient and the cerebrospinal fluid pressure. We found that many patients with severe intracranial injury and also suffering from severe shock usually occasioned by associated injury tended to have low cerebrospinal fluid pressures. Like other observers (2) we could not discern any consistent correlation between the patient's blood pressure, pulse or respiration and the cerebrospinal fluid pressure. Headache was usually relieved immediately by spinal drainage and although it was observed that intravenous hypertonic sucrose would often times accomplish this same result, its relief was much slower in appearance and much less prolonged.

**Surgical intervention.** The neurosurgery of all units during 1938-1939 and for all except



Graph 3. Delayed return to normal despite drainage.

3 cases during 1939-1940 was supervised by the same neurosurgeons, hence no attempt is made to separate the statistics by units. During the 2 year period 1939-1940 there were 16 compound skull fractures debrided with 3 deaths, 3 simple depressed fractures elevated with no deaths, 13 patients explored for surgical bleeding, and of this group only 1 presented the picture about which we bear so much, of so called "middle meningeal hemorrhage"—the remainder presenting the difficult diagnostic problem commonly seen in severe intracranial injury. Of the 13 cases explored, hematomas were found and evacuated in 8, of these 4 survived. In 5 extensive brain injury with diffuse bleeding was found and none survived.

In the group A cases there were 6 at post mortem which showed large hematomas, but of this group all died within 3 hours after admission without presenting localizing signs except 1. In this instance because of advanced age and the absence of localizing signs, it was deemed inadvisable to explore. In group B likewise, 4 at autopsy showed similar findings, 3 of whom died within 3 hours after admission, and 1 died on the fourth day after a diagnosis of cerebral apoplexy inaccurately made largely because of inadequate history.

It seemed of significance to us that we did not experience any increase on Unit B of hematoma formation due to the complete spinal drainage of grossly bloody spinal fluid which was carried out as some contend that spinal drainage in the presence of bloody spinal fluid will only facilitate increased

bleeding In several patients we made a partial replacement of the fluid removed by air injection into the spinal canal, but we could not state that there was any apparent effect on the continuation of the bleeding. This has been suggested by Fay (5) as a possible aid in the control of traumatic intracranial bleeding.

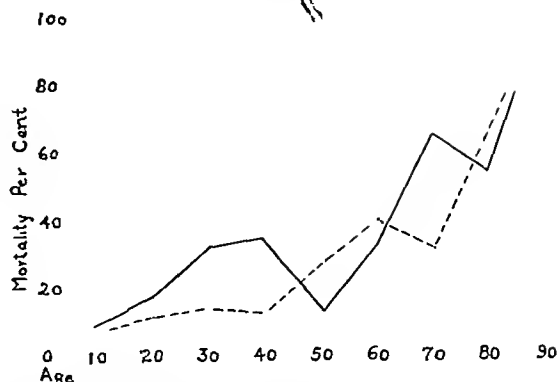
#### RATIONALE OF TREATMENT

The rationale of this mode of treatment has been beautifully expounded by Fay (4), but it is difficult to correlate it with the observations of Browder and Meyers. We have continued the regimen because of improved mortality and our very definite impression that patients were benefited by the treatment. We are not convinced that any one of the three, i.e., spinal drainage, hypertonic agents or limitation of fluids, is most important or absolutely essential, but we feel that all three have their indications.

A properly performed spinal puncture gives important diagnostic and prognostic information, is of definite value in the relief of traumatic headache, and, judging by our results, of definite value in the treatment of these patients.

Although Gurdjian and his co-workers state "the intravenous administration of isotonic fluids did not cause any increase in the cerebrospinal fluid pressure in the great majority of their cases" and advocate the administration of 2,500 to 3,500 cubic centimeters of fluid by vein in patients with severe intracranial injury who remain unconscious for days, we feel that the restriction of fluid intake to 1000 cubic centimeters per day for the first 48 hours was of definite aid in the treatment of these patients. After that in the type of case mentioned it is advisable to increase the fluid intake to 1,500 or 2,000 cubic centimeters because continued dehydration may produce untoward reactions. By marked fluid restriction to 500 cubic centimeters for 2 and 3 days in a few cases, we have had an opportunity to observe the "dry tap" as a result as previously described by Fay (4).

Schwartz and Elman have shown that sucrose is not as effective a dehydrating agent as is sorbitol, and the use of hypertonic



Graph 4 Mortality of groups "A" and "B" by decades  
A— B----

sucrose has been very recently questioned by Anderson and his co-workers, who found evidence of tubular damage in the kidneys after its use in patients with impaired renal function.

Unfortunately, in this regard almost all of these deaths were autopsied by the city coroner, who does not make routine microscopical examination of tissues, and hence sections of the kidneys are not available for review.

In 5 cases in which patients had received hypertonic sucrose autopsies were performed by the hospital pathologist, and Dr S H Gray states, "three of these showed marked swelling and vacuolization of the cytoplasm of the tubular epithelial cells. Nuclear changes were generally more markedly changed than the distal portions. Glomerular change was not noted except in a fourth case which showed general vascular congestion. In this case less tubular change was present. The patient who received the largest amount, 1,340 cubic centimeters of 50 per cent sucrose in the 96 hours preceding death, showed no renal lesion. The patient who received the smallest amount, 100 cubic centimeters of 50 per cent sucrose in the 24 hours preceding death, showed the most advanced tubular change."

Unless further observation shows that hypertonic sucrose produces the changes noted by Anderson in patients with normal kidney function, sucrose will probably continue to be used, since it is a valuable agent, easily and inexpensively prepared by the average hospital personnel.

## SUMMARY

1 A study of 121 cases of severe cranio-cerebral injury in which spinal puncture hypertonic sucrose and limitation of fluid intake were used in treatment is reviewed in this article.

2 A mortality of 23.1 per cent was experienced as compared with a previous 4 year mortality on this same unit of 36.7 per cent and as compared with a control unit (which used only hypertonic sucrose for 1 year and in addition the following year used limitation of fluid intake to 1500 cubic centimeters per day) which experienced a mortality of 34.1 per cent during this same 2 year period.

3 A decrease in the total hospital mortality during this 2 year period of 13.1 per cent over the average for the preceding 4 year period, or from 38.9 to 25.8 per cent.

4. In all deaths in patients treated by spinal drainage autopsies were carried out and in no instance did we observe any evidence of cerebellar herniation, medullary compression or "cone" formation. We attribute this to the slow removal of cerebrospinal fluid.

5 There was no increased hematoma formation in this group in which grossly bloody spinal fluid was "drained dry" nor is there any evidence that spinal drainage in these patients tended to increase or prolong hemorrhage.

6 Of 5 patients receiving hypertonic sucrose review of the kidney sections revealed that a man aged 27 years, who received 1,340 cubic centimeters of 50 per cent sucrose showed no renal lesion, while a man aged 50 years, receiving 100 cubic centimeters of 50 per cent sucrose showed the most marked tubular change.

## BIBLIOGRAPHY

- ANDERSON, W. A. D., and BROWN, W. R., J. Renal lesions following administration of hypertonic solutions of sucrose. *J. Am. M. Ass.* 940, 14, 981.
- a. BROWDER, JERRISON and MEYERS, R. *Ann. Surg.* 930, 337.
3. DIXON, WALTER E. Diagnosis and treatment of injuries of the head. *J. Am. M. Ass.* 913, 104, 77.
4. F. TENDLER. The treatment of acute and chronic cases of cerebral trauma by methods of dehydration. *Ann. Surg.* 1935, 106, 38.
5. F. TENDLER. *Surg. Clin. N. America*, 937, 1, 66.
6. GRA, S. H. Personal communication.
7. GORDIAN, E. S. WICKSTEIN, JONAS E. and SCHERER, CARL J. Studies on the spinal fluid in cases of injury to the head. *Arch. Neurol. & Psychiat.* 930, 43.
8. KARR, R. EMMETT. Personal communication.
9. SCHWARTZ, H. and KAMAR, R. Effect of sorbitol and sucrose on the cerebrospinal fluid pressure and urinary output. *Proc. Soc. Exper. Biol. & Med.* 938, 30, 506.
- a. STEWART, J. W. Fractures of the skull. *J. Am. M. Ass.* 9, 77, 3030.
1. WICKSTEIN, DRUMHART H. Drainage of cerebrospinal fluid in the treatment of acute head injuries. *Arch. Surg.* 937, 34, 42.
2. WORTS, B. S., and KENNEDY, FOSTER. A study of 100 cases. *Surg. Gynec. & Obst.*, 932, 33, 365, 370.

# THE PATHOGENESIS AND TREATMENT OF UNILATERAL EXOPHTHALMOS

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**A** PATIENT who presents himself to a neurological surgeon because of unilateral exophthalmos, failing vision, and inco-ordination of the extra-ocular muscles has usually been examined by one or more physicians, including an ophthalmologist. Thus the ophthalmologist perhaps has the greatest opportunity to discover the many conditions which may produce unilateral exophthalmos, among the more common of which are intra-orbital inflammatory disease—either primary or secondary to an infected paranasal sinus, paralysis of the extra-ocular muscles, cavernous sinus thrombosis, congenital anatomical defects, angiomas or aneurysms, either within or behind the orbit, and tumors of various types, also either within or behind the orbit. Judging from the available reports of both neurological surgeons and ophthalmologists concerning the causative lesions in unilateral exophthalmos, one gains the impression that vascular lesions and tumors are found more frequently by far. This has been true in our experience. Many of the patients have been referred to us after ophthalmological study elsewhere. It is with a discussion of these types of lesions that this paper is primarily concerned.

In a series of 604 verified and 150 unverified intracranial tumors, we have seen 15 patients with unilateral exophthalmos. Of these, 9 of the patients were males and 6 were females. The youngest in the group was a boy of 15 years, the oldest patient was a man of 59. All of these patients were referred to us by other physicians after the simpler causes of their visual difficulties had been ruled out, and in each case the eventual treatment proposed was surgical. The operative findings divided them into 3 groups: (1) unilateral exophthalmos with tumors, (2) unilateral exophthalmos with aneurysms, and (3) tumor

or aneurysm suspects, the lesion being unidentified. Other patients with various types of exophthalmos have been seen, but they do not fall into this particular surgical category and are therefore not included in this discussion.

Among this group of patients there were 7 who had intracranial tumors. In each case the exophthalmos was strictly unilateral and in no instance was it of the pulsating form. The tumors in 4 cases were meningiomas: 2 being global meningiomas of the sphenoidal wing and 2 being meningiomas of the optic nerve. One tumor still remains unclassified and the other was a glioma of the optic nerve.

The largest tumor of the group was a large spherical meningioma of the meningeothelial cell type, larger than a tennis ball, arising from the lateral portion of the right sphenoidal wing. At operation it was found that it did not extend past the midline to the left side. It lifted the frontal lobe up from its base and had also broken through the orbital roof. Growing forward behind the orbital roof it had produced almost complete immobility of the globe, and unilateral exophthalmos. Immediately after operation, after achieving removal of the tumor and of the roof of the orbit, the eye receded and on palpation and measurement there was a marked decrease in the tenseness and in the size of the eyeball. Verifying the position of the tumor of the skull, the bony orbital roof and lateral portion of the sphenoidal wing were found to be greatly thickened and irregular (Fig. 1).

The other global tumor, smaller than the one just described, was situated on the sphenoidal ridge and occurred within the Sylvian fissure. It completely isolated the tumor described in the first case. The dark, purple, meaty tumor was removed in its entirety with the aid of the surgical unit, but it was not possible to

and it was intimately attached to the underlying bone. The pterional and alar areas, as well as the lateral wall of the orbit were rough, thick, and very vascular when the dura mater was stripped free. The lateral wall and roof of the orbit were removed back to the optic foramen and the bony attachment of the tumor was thoroughly sparked with a desiccating current. This tumor proved to be an angioblastic meningioma, and sections of portions of the removed bone showed a rich infiltration of the tumor into the bone. The exophthalmos continued to recede for several weeks following the operation (Fig. 2).

The 2 patients with meningioma *ex plaque* had an exophthalmos of longer standing than did either of the two patients just described. In 1 of these patients the meningioma, being principally intra-orbital, presented itself at the enlarged optic foramen and extended sheet-like over the orbital contents just under the bony roof. Following removal of the tumor and a wide orbital decompression the patient's eye receded and his facial expression returned to normal. This tumor was the common variety of meningotheelial cell type with many small whorls of cells but no psammoma bodies (5). Though its location certainly suggests that the tumor arose in the sheath of Schwalbe slight impairment of visual acuity and moderate symmetrical contraction of the visual field in that eye speak against it.

The other patient, a middle aged colored woman, had the most marked exophthalmos of any patient in the series. The eye was completely blind and motionless, and there was an edema of the conjunctiva and lids of many months standing. At operation a thick sheet of very vascular tumor tissue was found to extend over the floor of the anterior and middle cranial fossae on the left side, centering about the clinoid processes and alar ridge. It was impossible to remove all of the tumor and when an electric burr was used in an attempt to open the orbital roof dense vascular bone was removed to a depth of over one inch without even reaching the space of the orbit. The bone of the sphenoidal wing and the immediately adjacent cranial floor was everywhere rough, greatly thickened, and extremely bloody when it was rongeured or

stripped of either tumor tissue or dura mater. Following the operation there was a distinct improvement in the edema of the conjunctiva and eye lids, but the exophthalmos remained unchanged. This tumor likewise meningotheelial in type, contained many vascular sinuses, large and small nests or whorls of cells, and many fine psammoma bodies (Fig. 3).

Another patient developed complete loss of vision marked proptosis, and paralysis of the extra-ocular muscles on the right, over a period of only 3 months. At operation he was found to have a highly vascular mass of tissue which occupied the chiasmal region, and extended laterally over the clinoid processes, the sphenoidal wing and the posterior half of the roof of the orbit. An extension of the tumor was also found in the greatly enlarged optic foramen. The patient withstood the operation very well, and a large portion of the tumor was removed, but on the third day he suddenly became comatose and expired within a few minutes. At autopsy many nodules from the size of small shot to that of a large grape were found over the basal dura mater particularly clustered about the foramina of exit of the cranial nerves. One could insert the tip of a finger into the optic foramen, and the orbital roof everywhere paper thin, was completely absent in one area 3 by 2 centimeters. There was no intra-orbital mass. Several pathologists have studied sections of both the main tumor mass and the scattered nodules. They all show the same tumor tissue, but to date it has not been classified. It is most likely however a carcinoma of some unusual type, possibly metastatic, though a complete autopsy did not reveal a primary lesion elsewhere in the body.

The remaining patient with a tumor was a boy of 15 who had an exophthalmos and complete blindness of the left eye. There were no other neurological findings, and the roentgenological studies of the orbits showed optic foramina of equal size. Nevertheless, it was suspected that he had a glioma of the optic nerve, and upon operation a large mass was found to obscure the left optic nerve and optic foramen completely. When the capsule was incised preparatory to its removal, soft granular tissue oozed from the opening. At

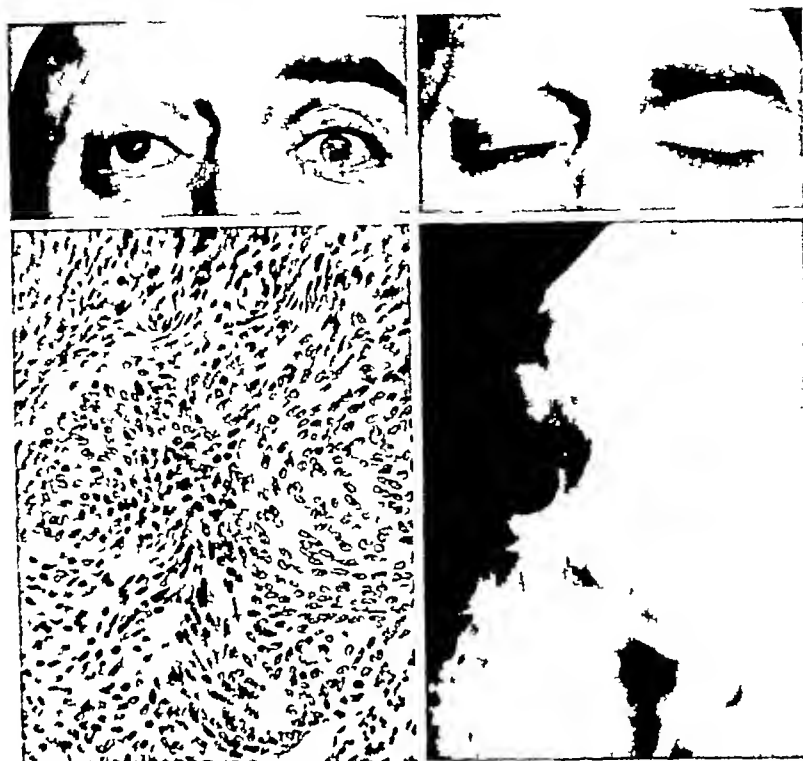


Fig 1 A large, solid meningioma arising from the right sphenoidal wing produced a homolateral non pulsating exophthalmos, shown here in the patient at the time of operation. There was a marked thickening of the bone of the sphenoidal wing and orbital roof. The tumor is of the meningothelial cell type, with but little reticulin formation, and with a tendency to form large whorl patterns.

that moment tremendous arterial hemorrhage occurred and only after a desperate struggle was it brought under control. Unfortunately, no tissue was obtained for histological verification. The boy's recovery was good and his exophthalmos has receded, probably because of the cranial decompression opening which was made at the time of operation.

Here, then, are 6 examples of unilateral exophthalmos with other variable neurological symptoms, occurring in the presence of a variety of tumors in or immediately behind the orbit. As will be pointed out later, the tumor type, its exact location, its duration, and its effect on the bones of the cranial fossae are matters of importance in an understanding of the mechanism of the exophthalmos.

Included in this series are 4 patients with aneurysms. One patient, a woman of 48

years, presented an exophthalmos together with other cranial nerve symptoms which led to a diagnosis of a right sided paratrigeminal lesion. Blood was found in her cerebrospinal fluid, and it was believed that her symptoms were due to a bleeding aneurysm of the intracranial portion of the internal carotid artery. Her protruding eye did not pulsate, and an intracranial bruit was not definitely verified. She left the hospital without treatment and has since died elsewhere without an autopsy having been performed.

Another patient, a woman of 41 years, developed a pulsating unilateral exophthalmos of the right eye over a period of several years, with no preceding history of trauma to the head. The eye protruded markedly, so that it was estimated that 50 per cent of the sclera was exposed. The lids were purple, edematous, and thickened with a tangled subcutaneous



Fig. 2. The thickening of the alar and pterional bone, as well as that of the posterior orbital area, locates the site of the globular excursions of angioblastic type which infiltrated the underlying vascular hyperplastic bone. The vascular sinuses of the tumor are lined by flattened and endothelial cells. Also the solid portions are composed of large polyhedral meningiomatous cells. The photograph of the patient shows her condition on discharge after operation, here there is already marked recession of the exophthalmos.

mass of tortuous small veins. The scleral vessels were large and pulsating. There was only a slight limitation of the motion of the eyeball, however, and there was no diplopia. Visual acuity of the affected eye was 20/40 of the left eye 20/50. The supra-orbital angular, nasal, and facial veins were visible without palpation and were as large as a common lead pencil. There was a thrill and bruit through

out the skull and right side of the face. The eye actually bounded with the pulse. It was impossible to obliterate completely the pulsations and bruit by digital pressure in the neck, though the patient stated that when such pressure was applied she herself could no longer bear the bruit. At operation the right external carotid and right common carotid arteries were ligated after it was found that

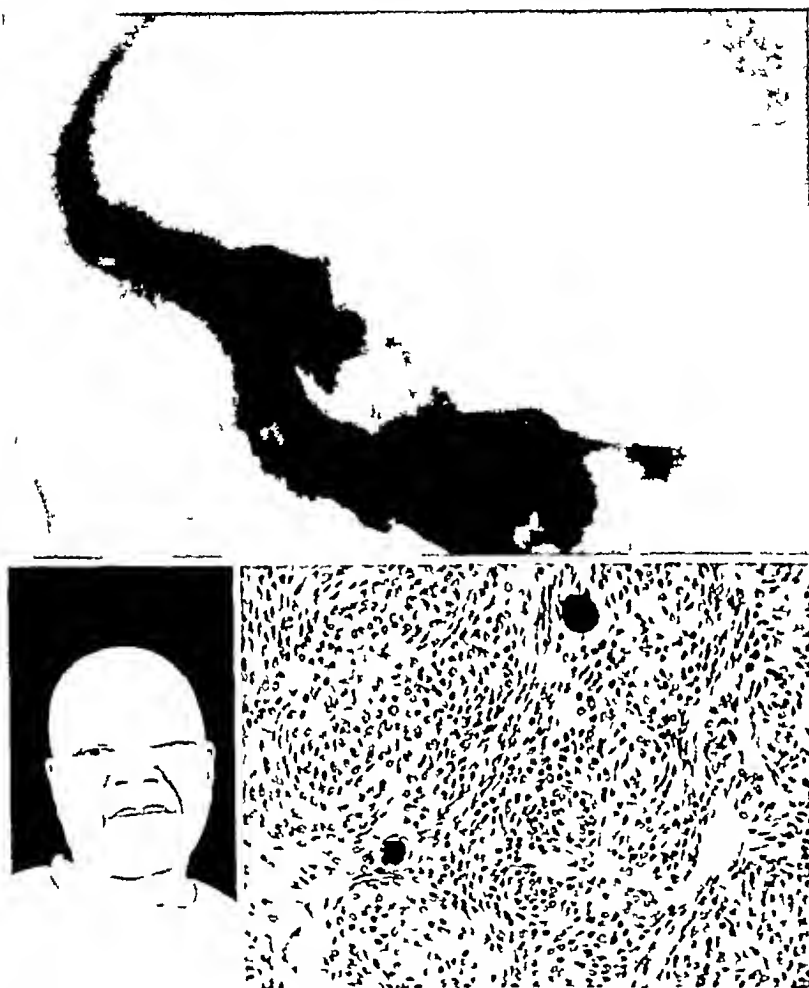


Fig 3 This meningioma *en plaque* of long standing caused a tremendous thickening of the sphenoidal wing as well as of the orbital roof and the floor of the middle cranial fossa. It is a meningotheelial meningioma of low reticulin content, containing psammoma bodies and showing well defined small whorl patterns. The patient is shown just before operation, when edema of the lids was so severe as to cover in most part the markedly exophthalmic left eye.

their temporary occlusion produced no signs of cerebral embarrassment. The jugular vein was unusually large but the carotid artery was of normal size. No communication between the two in the neck was seen. Following the ligation there was a complete and immediate cessation of the bruit, pulsations were gone in the cheek, in the angle between the eye and nose and over the forehead and the eye not only ceased to pulsate but it receded remarkably into the orbit. The scleral and palpebral vessels were greatly diminished in size and, in

fact the patient's facial expression was changed in great measure. It is possible, however, that due to the many possibilities of arterial and venous communication in this patient the internal carotid may eventually require ligation to give a permanent result (Fig 4).

Two other patients, both men about 38 years old and both with a protruding pulsating left eye had a history of trauma to the head immediately preceding the onset of their exophthalmos. The one patient developed a





Fig. 4. An arteriovenous aneurysm caused the right eye in this patient to bound with the pulse and to protrude markedly from the orbit. The large supra-orbital, angular and facial veins, the smaller tangled masses of veins on the upper lid, and the dusky purplish sclera with its dilated vessels, all added to the grotesque appearance of the face. Though the exact point of arteriovenous communication was not determined, ligation of the right common carotid and right external carotid arteries caused great decrease in the protrusion and prominence of the veins, as well as cessation of the loud bruit. The upper two photographs were taken before operation; the lower two show the improvement after ligation of the carotids.

prominence and pulsation of the left eye 4 months after having been struck in the left occipital region by a brick. He became conscious of a pounding whirring head noise, increased on exertion 6 months after the injury, and he developed a diplopia on looking to the left, in 7 months. His left eye was very prominent, it pulsated synchronously with the pulse and the scleral and palpebral vessels were engorged and tortuous. Following liga-

tion of the common carotid artery the pulsations ceased, the eye receded, and the engorgement of the scleral and palpebral vessels disappeared without the development of any neurological complications (Fig. 5).

The second patient was pinned between the floor of a garage and a motor which fell from its frame while he was working beneath an automobile. In addition to his left-sided pulsating exophthalmos, which developed 1



Fig 5 Struck in the left occipital region by a brick, this man, 4 months later, developed a left sided pulsating exophthalmos, dilatation of the scleral vessels, and a loud bruit. The upper pictures show his condition before operation, and the lower photographs show his eyes postoperatively when, after ligation of the left common carotid artery, his exophthalmos receded, the scleral vessels returned to normal, and the bruit disappeared

month following the injury, this man had a paralysis of various cranial nerves, including a unilateral facial paralysis. He complained of constant head pains and head noises. It was believed that he, like the preceding patient, had an arteriovenous aneurysm of the internal carotid artery and cavernous sinus. The left common carotid artery was ligated first, and a few days later the left external carotid was likewise tied off. One week following ligation of the external carotid the patient suddenly lost his speech and the power to move his right arm. He recovered in 2 or 3 minutes, and after a period of 5 minutes again lost his speech, which defect has remained permanently. Upon discharge his exophthalmos had improved greatly, and peri-orbital and scleral engorgement had disappeared, and he no longer complained of head noises, (Fig 6)

Three other patients were seen, all of whom had a unilateral, nonpulsating exophthalmos without other significant neurological symptoms. After careful neurological and roentgenological examination they were believed to have retro-orbital or intra-orbital tumors and were, accordingly, operated upon. No tumor was found at any place in the anterior or mid-

dle cranial fossa nor toward the midline about the chiasm and sella and in these patients the bone of the roof of the orbit and the sphenoidal wing was only moderately thickened. In each case the roof of the orbit was removed, and in each case the orbital contents rose into the decompression opening due to an apparent increase of intra-orbital tension. No tumor within the orbit was found in any of these 3 patients. In each patient decompression of the orbit relieved the exophthalmos and restored the facial expression to a normal state.

The 2 remaining patients, both with a left sided, non-pulsating exophthalmos with scleral and palpebral venous engorgement and pupillary fixation in dilatation, were believed to have tumors in the orbit or intracranially behind the orbit, but both refused operation and they have not been seen in follow-up examinations.

#### ANALYSIS

Six patients have been shown at operation to have tumors in or behind the orbit, with a co-existing, non-pulsating, homolateral exophthalmos. All 6 showed definite x-ray evidence of a tumor, in the thickening of the sphenoidal



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The second patient was pinned between the floor of a garage and a motor which fell from its frame while he was working beneath an automobile. In addition to his left-sided pulsating exophthalmos, which developed 1

upon exertion X-ray evidence of the aneurysms was lacking in every case, though we have seen positive evidence of bone erosion and deposits of calcium in other patients with aneurysms of the internal carotid. In 3 of our 4 cases the exophthalmos was pulsating, and in all the patients the prominence of the palpebral veins, the dilatation of the scleral vessels, and the increased lacrimation were much more marked than they were in the patients with tumors. Moreover, the exophthalmic eye was a much more startling object to behold. Certain other patients who have been seen with aneurysms, but without exophthalmos, have had a papilledema as well as a bruit, both of which improved following various combinations of carotid artery ligation.

In investigating the reports of others in their experience with unilateral exophthalmos, one is confronted by a variety of opinions as to the causes of, and the mechanics important in, such a condition. Randolph believed that sarcoma was by far the most common form of intra-orbital tumor, and he cited it as a prominent cause of unilateral exophthalmos, but he did not analyze any cases of retro-orbital tumors. In a series of 807 intracranial tumors reported by Elsberg, Hare, and Dyke, 15 patients had unilateral exophthalmos. Of these 15, 10 patients had meningiomas. There were 2 osteomas, 1 adenoma, 1 epidermoid, and 1 "Paget's disease with tumor." These men did not believe that venous stasis, which could be supposed to result from local or generalized increase of pressure, is a cause of exophthalmos. They never saw such a condition in any of their patients, and neither have we. Such a mechanism has not been satisfactorily demonstrated in animals in which attempts have been made experimentally to produce exophthalmos. In accord with our own observations, they noted that in most of their patients limitation of the eyeball was in all directions as a rule, but the degree of impaired motion was not necessarily in direct proportion to the degree of protrusion. They believed that the exophthalmos was most often due to a perforation of the tumor into the orbit, thickening of the orbital walls, extension of the tumor from the cranial cavity through the orbital tissues or optic foramen,

or a transference through these openings of the increased intracranial pressure. Our experience with 6 patients completely substantiates this explanation for the mechanisms of production of unilateral exophthalmos in patients of this category.

The degree of exophthalmos in the presence of a meningioma depends upon the degree of encroachment upon the orbital space by the hyperostosis of the bony walls of the orbit, and upon the bulk of tumor tissue which has grown into the orbit either by means of erosion or through the natural foramina of the orbit. We can accept, without specific data to support such a contention, the theory that the venous return flow of blood must be embarrassed to a certain degree under such conditions, and that there may well be an increase in the fibrous content of the fatty tissues surrounding the globe and muscles. We do not believe that Mueller's muscle is a factor in the production of unilateral exophthalmos in the human subject. Optic nerve gliomas characteristically produce an enlargement of the optic foramen through which they may grow forward, but not all optic gliomas produce an exophthalmos. Though apparently it is not commonly true, yet it is possible that a tumor, neither meningioma nor optic glioma, may produce unilateral exophthalmos when it lies behind the orbit. Our 1 unclassified tumor in this group caused no bony change other than erosion of the roof of the orbit and optic foramen, through which openings it grew into the orbit, pushing the orbital contents before it. The closer to the orbit the site of primary tumor growth, the earlier will be the appearance of the exophthalmos, and accordingly, the tumor of long standing will have caused a greater degree of exophthalmos than the tumor of recent growth.

Sugar and Meyer, commenting upon the exophthalmos in the presence of aneurysms, state "Of the several anatomic causes of pulsating exophthalmos the most frequent is traumatic rupture of the internal carotid artery in its passage through the cavernous sinus." They point out that aneurysms may be traumatic, luetic, arteriosclerotic, or congenital. They explain the mechanism of the exophthalmos as follows:

After rupture of the internal carotid artery, there is an overflow of arterial blood into the venous sinus with consequent increase in the venous pressure and reversal of venous flow in the ophthalmic veins and their tributaries. The resulting stasis, edema, and increase in blood volume in the venous bed produce exophthalmos. Through the dilated venous channels the arterial pulsation is transmitted to the eyeball and orbital tissues. Since the ophthalmic veins are the only tributaries of the cavernous sinus which have no dense tissues around them, such as is present around the intracranial venous sinuses, they may dilate and give rise to the pulsating large venous masses often seen at the internal angle of the eye, usually consisting of the superior ophthalmic vein formed by the union of the supra-orbital and angular veins."

Cushing and Bailey do not report any case of pulsating exophthalmos in the presence of an angioma arteriale, nor have any patients with an arterial or venous angioma of the cerebrum or cerebellum in our series been observed to have a pulsating unilateral exophthalmos. They do point out, however, that though no pulsation is seen in the eye in such patients, frequently a bruit can be heard when the globe is auscultated when an angioma arteriale is present in the brain, and that therefore a unilateral exophthalmos with audible bruit in the globe need not necessarily be an infallible sign of arteriovenous fistula between the carotid and cavernous sinus. Such a matter of differential diagnosis is important, for the treatment of arteriovenous aneurysms and of arterial or venous angiomata is quite different.

Smelser produced exophthalmos in thyroidectomized guinea pigs by the injection of pituitary extract but unilateral or bilateral extirpation of the cervical sympathetic ganglia did not affect the exophthalmos. These animals had been prepared previously by the removal of Mueller's muscle (a large muscle in the guinea pig) and the exophthalmos persisted even after death. Therefore such exophthalmos could not be due to continuous sympathetic stimulation or the direct result of continued contraction of Mueller's muscle. He did find, however, a hypertrophy of the

periglobal soft tissues. It would be difficult to explain the exophthalmos seen in our patients on the basis of overactivity of the sympathetic, and the muscle of Mueller is too small a structure in man to tilt the eye outward, and it seems improbable that it could cause such marked venous stasis by its contraction. That a fibrous tissue hypertrophy would result, Skydsgaard agrees that the exophthalmos present in patients with intracranial tumor is not due to sympathetic stimulation.

Many a neurological surgeon has had the opportunity to observe patients with intracranial tumors and aneurysms who did not have an exophthalmos. Large retro-orbital tumors, such as those large old chromophobe adenomas of long standing that may reach laterally and anteriorly far beyond the simple confines of the sella turcica or the large tumors of the under surface of the temporal lobe which push forward toward the orbit, are of common occurrence, but they do not cause unilateral exophthalmos. A terrific increase in intracranial pressure such as follows the rapid growth of certain tumors of the posterior cranial fossa, does not produce unilateral exophthalmos. Other possible causes for the exophthalmos having been eliminated, one must always suspect a retro-orbital tumor either confined within the intracranial cavity or actually growing into the orbital space or an arteriovenous aneurysm. If the lesion be a tumor there will usually be confirmatory roentgenological evidence. If be an aneurysm, there may or may not be roentgenological findings, there will usually be a bruit on the involved side, there may be history of trauma and there is a striking engorgement of the palpebral and scleral vessels. The exophthalmos will more than likely pulsate when an aneurysm is present, whereas it will be non-pulsating when caused by tumor.

The treatment of unilateral exophthalmos, whether due to tumor or aneurysm, is surgical. The tumor must be removed as completely as possible, both its intracranial and intracranial portions, and all bone which has been invaded must be removed, where this is feasible to prevent a recurrence. The bone removal is especially important where a fair



# THE TREATMENT OF DIFFUSE PERITONITIS BY THE DIRECT INTRAPERITONEAL INTRODUCTION OF SULFANILAMIDE

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EVER since the more recent work on the therapeutic activity and mode of action of sulfanilamide there have been various reports on the effects and methods by which sulfanilamide achieves its results, for the most part, on beta hemolytic streptococci. All authors have stressed the fact that there is no bactericidal effect in the sense that an antiseptic like iodine might attack infective organisms. This we feel has given rise to the general impression that in order to be effective in a specified local area, sulfanilamide must be given systemically. It is our impression not yet definitely proved, that when sulfanilamide can be utilized locally—such as in the peritoneal cavity—and the concentration maintained at the proper level the same therapeutic result and even a better result may be obtained than by its pure systemic use.

Long and Bliss (7) in one of their original articles showed that sulfanilamide in certain concentrations when placed in contact with cultures containing beta hemolytic streptococcus definitely inhibited multiplication of the organisms.

Colebrook and Kenny (2) have pointed out that the serum of a patient ill with streptococcal puerperal sepsis becomes increasingly bacteriostatic to the organism after multiple doses of protosil. Long and Bliss were unable to verify this work, partly due to the fact that human serum is often bactericidal to strains of streptococci. It is probable that statements such as that of Colebrook and Kenny have been to a great extent responsible for the lack of utilization of sulfanilamide as a local agent in the treatment of various infections.

Domagk, in his original paper made note of the importance of phagocytosis in the action of sulfanilamide. Levaditi and Valsman attributed this increase in phagocytosis to the interference with the bacterial capsule formation.

Long and Bliss (8) conclude that there is no bactericidal effect in the action of sulfanilamide and moreover definitely decide that the serums of patients treated with sulfanilamide exert little if any bactericidal effect on beta hemolytic streptococci. They feel that there is a definite bacteriostatic effect *in vivo* as well as *in vitro* and ascribe to phagocytosis the so called clean-up rôle.

The fundamental observations of Marshall show that sulfanilamide is quickly absorbed when it is administered orally or parenterally. He has shown that it becomes distributed with surprising uniformity throughout all the tissues, including the tissues of the infected site.

Colebrook, Battle, and O'Meara (1) have definitely shown that it made no essential difference whether the sulfanilamide-laden blood was obtained from a treated patient or through the addition of the chemical to normal blood. They both had the property to kill beta hemolytic streptococci and prevent their multiplication *in vitro*.

J. S. Lockwood (5) has beautifully demonstrated that phagocytosis is not necessary (*in vitro* at least) to interfere with bacterial growth. Interference takes place to the same extent in human serum which contains no phagocytes. Moreover he has also shown that the presence of peptone is important in the action of sulfanilamide. He thus concluded that sulfanilamide acts upon hemolytic streptococci by interference with their protein digesting mechanism. This accounts for the fact that sulfanilamide is of greatest

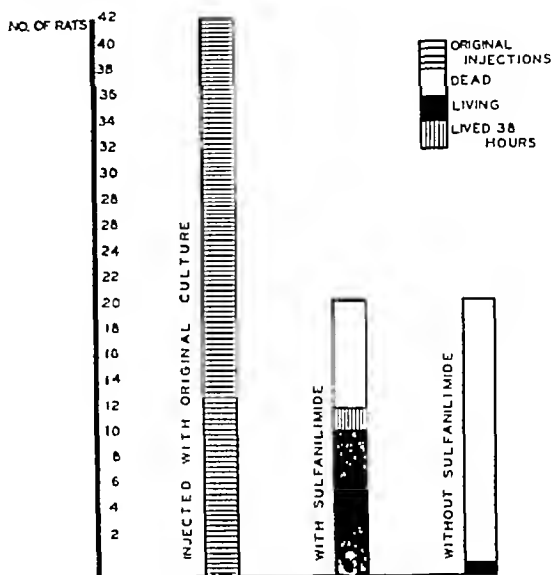
From the Surgical Service of Herbert Froehne, M.D., and Isaac Kaufmann Foundation of the Montefiore Hospital, Pittsburgh, Pennsylvania.

value in lesions in which there is a minimum of tissue destruction

In a later rather extensive and detailed report Lockwood (6) comes to the following conclusion "It is possible that sulfanilamide combines in some way with the free amino-nitrogen of protein degradation products and renders them unsuitable for bacterial utilization", thus allowing the bacteria to die literally by starvation. This concept would appear to explain why the sulfanilamide compounds are active only against certain organisms. It begins to appear that sulfanilamide is not so much specific against any organism *per se* as it is particularly beneficial against any organism which is not protected by a strong wall composed of proteolytic products. Thus it is known that sulfanilamide is not effective against hemolytic streptococci in abscesses, but may be effective against staphylococcus in the presence of a staphylococcal cellulitis.

This preliminary survey brings us to our main thesis: *the local application of sulfanilamide to the healing of infected tissues*. We have tried to bring out the fact that the main idea of sulfanilamide therapy is to secure an effective concentration of sulfanilamide or possibly a direct derivative at the infected site. We reason then, that sulfanilamide should be utilized locally in high concentration whenever practical. We cannot understand why this particular phase of sulfanilamide therapy should have been pushed into the background. If unmodified sulfanilamide is the effective agent, one should logically be able to utilize it in this manner and if an oxidation product is the active agent, there is no reason why this cannot be formed in a wound such as a granulating cavity or inflamed peritoneal surface. If Lockwood's experiments have good foundation, and we have every reason to believe that they have, then the most important aim in parenteral therapy is to get a high concentration of sulfanilamide at the infected site. Surely this can often be obtained more easily by local introduction than by the systemic route.

It occurred to us that the peritoneum would be an ideal site to test this theory. If, on encountering a diffuse or localized peritonitis at operation, one could instill sulfanilamide in the form of a crystalline product before closing



Graph 1 Experiment 1

the peritoneal cavity, one might then have a definite protection against the further spread of the process, provided the focus were removed. In no way do we wish to deprecate the valuable effect of sulfanilamide given subcutaneously in the treatment of peritonitis, for we know it to be of inestimable importance. However, it is our feeling that sulfanilamide, when introduced into the peritoneal cavity in the form of a crystalline powder and subsequently reinforced by subcutaneous introduction of a 0.8 per cent solution of sulfanilamide, is a definite advance in our armamentarium against the ravages of peritonitis. We know certainly that the sulfanilamide introduced into the inflamed peritoneal cavity of humans, permeates the tissues rapidly and is found in the blood stream soon afterward in a fairly high concentration. It is in all probability re-excreted into the peritoneal cavity as well as other tissues. Inasmuch as the number of cases of generalized peritonitis any one man can have is limited we felt that if we could reproduce in rats the conditions found in human peritonitis, we might have some justification for our clinical impression, and thus perhaps encourage others to utilize sulfanilamide in this way.

In our experiments we have made our problem rather difficult by selecting no particular



TABLE L.—THE EFFECT OF SIMULTANEOUS INJECTION OF POSITIVE CULTURES AND SULFANILAMIDE POWDER INTO THE PERITONEAL CAVITY OF RATS, DURING THE PERIOD OF FEBRUARY 1 1940 TO MARCH 14 1940

No	Date of injection	Culture	Amount cm	Sulfanilamide		Result	Post-mortem examination	Post-mortem culture
				Amount in mgm	Route			
	2-1-40	Strep. B coli		None		Dead 20 days	Peritonitis	Strep. B coli
	2-4-40	Strep. B coli		50	I P	Living		
	2-7-40	Strep. B coli		None		Dead 24 hours	Early peritonitis	Strep. B coli
	2-7-40	Strep. B coli		100	I P	Dead 1 hour	Early peritonitis	Strep. B coli
5	2-13-40	Strep. B coli	5	None		Dead 1 hour	Kochman, peritonitis	Strep. B coli
6	2-13-40	Strep. B coli		100	I P	Living		
	2-14-40	B coli Exsura		None		Dead 24 hours	Kochman, peritonitis	Exsura B coli
8	2-14-40	B coli Exsura		100	I P	Dead 1 hour	Early peritonitis	Strep. B coli
	2-14-40	B coli Strep		None		Dead	Early peritonitis	B coli Strep
10	2-14-40	B coli Strep	11	50	I P	Living		
	2-18-40	B coli Strep		None		Dead	Mildly peritonitis, dilated stomach	B coli Strep
12	2-18-40	B coli Strep	11	100	I P	Living		
	2-27-40	Strep. B coli	15	None		Dead	Exudative peritonitis	Strep. B coli
14	2-27-40	Strep. B coli		100	I P	Living		
	2-28-40	Strep. B coli		None		Dead	Peritonitis	Strep. B coli
16	2-28-40	Strep. B coli		100	I P	Dead	Peritonitis	Strep. B coli
	2-28-40	Strep. B coli		None		Dead	Peritonitis	Strep. B coli
18	2-28-40	Strep. B coli		100	I P	Dead	Peritonitis	Strep. B coli
19	2-12-40	B coli Gram positive diplococci	15	None		Dead	Peritonitis	B coli Gram positive diplococci
20	2-12-40	B coli Gram positive diplococci		50 50 (in lots)	I P	Living		
21	2-12-40	B coli		None		Dead	Peritonitis	B coli Gram positive diplococci
22	2-12-40	B coli		100	I P	Dead in interval—exam done after sulfanilamide	Peritonitis clear	B coli Gram positive diplococci
	2-16-40	B coli Gram positive diplococci	15	None		Dead Overdosed	Peritonitis—mildly limited	B coli Gram positive diplococci
24	2-16-40	B coli Gram positive diplococci	15	50	I P	Living		
25	2-17-40	Gram positive diplococci coli	33	None		Dead	Focal mottling peritonitis	Gram positive diplococci B coli
26	2-17-40	Gram positive diplococci B. coli	33	100	I P	Dead	Peritonitis looked clean	Gram positive diplococci B. coli
27	2-22-40	Gram positive diplococci B. coli	4.33	None		Dead	Focal peritonitis	Gram positive diplococci B. coli
28	2-22-40	Gram positive diplococci B. coli	33	100	I P	Dead	No color—peritonitis looked clean	Gram positive diplococci B. coli
29	2-20-40	Gram positive diplococci B. coli	4.33	None		Dead	Dilated bowels	Strep. B coli
30	2-20-40	Gram positive diplococci B. coli	4.33	50	I P	Living		

-Strep. B. coli = Strep. B. coli I. P. = intraperitoneal

TABLE I—THE EFFECT OF SIMULTANEOUS INJECTION OF POSITIVE CULTURES AND SULFANILAMIDE POWDER INTO THE PERITONEAL CAVITY OF RATS, DURING THE PERIOD OF FEBRUARY 1, 1940 TO MARCH 14, 1940—Continued

No	Date of injection	Culture	Amount c cm	Sulfanilamide		Result	Postmortem examination	Postmortem culture
				Amount in mgm	Route			
31	2-21-40	B coli	0.3	None		Dead	Peritonitis	B coli
32	2-21-40	B coli	0.3	50	I P	Dead	Peritonitis	B coli
33	2-28-40	Strep B coli	0.3	None		Dead	Peritonitis	Strep B coli
34	2-28-40	Strep B coli	0.3	50 25	I P	Living		
35	3-9-40	B coli Strep	0.3	None		Dead	Foul peritoneal exudate	B coli Diplococci Strep
36	3-9-40	B coli Strep	0.3	75 75 75	I P	Living		
37	3-10-40	B coli	0.4	None		Living		
38	3-10-40	B coli	0.4	75	I P	Dead	Peritonitis	B coli
39	3-12-40	Strep B coli	0.4	None		Dead	Peritonitis	B coli Strep
40	3-12-40	Strep B coli	0.4	75 75	I P	Dead 36 hours later		B coli
41	3-14-40	Strep B coli	0.4	None		Dead	Peritonitis	Strep B coli
42	3-14-40	Strep B coli	0.4	75 75	I P	Living		

Strep, streptococcus  
I P intraperitoneal

organism. Cultures were taken from the aspirated contents of acute suppurative appendices or from the peritoneum of peritonitis cases. We felt that the human peritoneum has no chance to select the particular organism which invades it and in this sense we might reproduce the situation in the rat. Thus, varying amounts of different cultures were injected intraperitoneally into two rats, one of which was given a simultaneous intraperitoneal injection of sulfanilamide suspended in saline. The control rat was given a corresponding amount of saline intraperitoneally to equalize any factor of dilution. The results are tabulated in Table I.

In this series of 42 white rats injected subcutaneously with varying amounts of cultures consisting for the most part of *Bacillus coli*, *Streptococcus nonhemolyticus*, and gram positive diplococci, 20 of a possible 21 unprotected rats died in various stages of peritonitis. In contrast to this 11 of 21 rats protected by intraperitoneal sulfanilamide lived indefinitely. One rat died in convulsions, apparently from an overdose of sulfanilamide and 1 died 36

hours after the unprotected rat. We emphasize that the conditions of the experiment were rather severe inasmuch as a variety of organisms were introduced and the streptococcus was at no time of the beta hemolytic type. Perhaps if only one organism were used the results would have been even more striking. The results are expressed in Graph 1.

In the second phase of the study an even more rugged type of experiment was set up. An attempt was made more faithfully to reproduce the situation met with in human peritonitis. In other words sulfanilamide was not introduced for varying lengths of time following the intraperitoneal injection of mixed cultures and consequently a peritonitis of varying duration was present when sulfanilamide was introduced. Another variation was introduced in that, in addition to instilling the drug intraperitoneally another rat was utilized for the subcutaneous administration of a similar dose. Thus an attempt was made to show that the intraperitoneal route has advantages or disadvantages over the subcutaneous route in the administration of sulfanilamide. It

TABLE II.—THE INJECTION OF INTRAPERITONEAL SULFANILAMIDE POWDER AND SULFANILAMIDE SOLUTION IN ADVANCED PERITONITIS OF RATS, DURING PERIOD OF MARCH 23 1940 TO APRIL 28, 1940

No.	Date	Culture	Amount in ccs	Description of peritonitis	Sulfanilamide		Result	Postmortem examination	Postmortem culture
					Amount in mgm	Route			
1	3-23-40	B coli Dip B pyocyaneus Scrap.		4 hrs	None		Dead 24 hrs	Peritonitis	B coli Scrap B pyocyaneus
2	3-23-40	B coli Dip B pyocyaneus Scrap		hrs	do do do do 24 hr intervals	I P	Living		
3	3-23-40	B coli Displaced pyocyaneus Scrap		hrs	do do do do 24 hr intervals	B Q	Living		
4	3-25-40	B coli Scrap pyocyaneus		6 hrs	None		Dead 24 hrs	Full blown peritonitis	B coli Displaced B pyocyaneus
5	3-25-40	B coli Scrap pyocyaneus		6 hrs	100 mg do do 5	I P	Dead 2 days after injection	Abdominal wall Adhesions	B coli Displaced
6	3-25-40	B coli Scrap B pyocyaneus		hrs		B Q	Dead 36 hrs	Peritonitis	B coli Displaced B pyocyaneus
7	3-26-40	B coli Scrap B pyocyaneus		16 hrs	None		Dead 24 hrs	Peritonitis	B coli Scrap Lungs
8	3-26-40	B coli Scrap B pyocyaneus	2	16 hrs	100 mg do 24 hr intervals	I P	Living		
9	3-26-	B coli Scrap pyocyaneus		16 hrs	100	B Q	Dead 24 hrs	Peritonitis	B coli pyocyaneus
10	3-27-40	B coli Scrap. B pyocyaneus		16 hrs	None		Dead in 20 days (Lungs enlarged)	Abdominal adhesions, size of peritonitis	B coli Displaced
11	3-27-40	B coli Scrap. B pyocyaneus		16 hrs		I P	Dead in 6 days (2 days longer than B Q)	Peritonitis	
12	3-27-40	B coli Scrap. B pyocyaneus		16 hrs		B Q	Dead in 24 hrs	Final-stage peritonitis	
13	3-27-40	B coli Scrap B pyocyaneus	0.4	16 hrs	None		Dead in 36 hrs	Early peritonitis	Diphtheria B coli Scrap pyocyaneus
14	3-27-40	B coli Scrap B pyocyaneus		16 hrs	100 mg do 24 hr intervals	I P	Living		
15	3-28-40	B coli Scrap B pyocyaneus		16 hrs	100 mg do 24 hr intervals	B Q	Living		
16	4-1-40	B coli Scrap	0.2	hrs	None		Dead in 24 hrs	Peritonitis	B coli Scrap
17	4-1-40	B coli Scrap	0.2	6 hrs	do do do do 24 hr intervals	I P	Dead in 24 hrs (Weak, then nil)	Peritonitis (peritonitis?)	B coli Scrap Scrap
18	4-1-40	B coli Scrap	0.25	hrs	do do do do 24 hr intervals	B Q	Living		
19	4-1-40	B coli Scrap.	0.2	hrs.	None		Distention	Distention	B coli Scrap.

B Q subcutaneous.

TABLE II—THE INJECTION OF INTRAPERITONEAL SULFANILAMIDE POWDER AND SULFANILAMIDE SOLUTION IN ADVANCED PERITONITIS OF RATS, DURING PERIOD OF MARCH 23, 1940 TO APRIL 28, 1940—Continued

No	Date	Culture	Amount c.cm	Duration of peritonitis	Sulfanilamide		Result	Postmortem examination	Postmortem culture
					Amount in mgm	Route			
20	4-2-40	B coli Strep	0.25	6 hrs	80 80 24 hr intervals	I P	Living		
21	4-2-40	B coli Strep	0.25	6 hrs	80	S Q	Dead 30 hrs	Early peritonitis fluid	B coli Strep
22	4-3-40	Strep B coli Entero B pyocyaneus	0.3	8 hrs	None		Dead 4-12-40 (2 days longer than S Q)	Abdominal wall abscess	B coli B pyocyaneus Entero
23	4-3-40	B pyocyaneus Strep B coli Entero	0.3	8 hrs	80 80 80 40 40 4-12-40	I P	Dead 4-19-40 (9 days longer than S Q)	Peritonitis-abscess	B coli Strep
24	4-3-40	Strep B coli Entero B pyocyaneus	0.3	8 hrs	80 80 80	S Q	Died 10 24 hrs	Peritonitis	Entero B coli B pyocyaneus Diplococci
25	4-4-40	B coli Strep. Entero	0.3	8 hrs	None		Living		
26	4-4-40	B coli Strep Entero	0.3	8 hrs	80 80 24 hr intervals	I P	Living		
27	4-4-40	B coli Strep Entero	0.3	8 hrs	80	S Q	Died 24 hrs	Severe peritonitis	Strep B coli Entero
28	4-6-40	B coli Strep Entero	0.5	20 hrs	None		Died 4-20-40 (9 days longer than S Q)	Severe peritonitis	B coli Entero
29	4-6-40	B coli Strep Entero	0.5	20 hrs	80 80 24 hr intervals	I P	Lived		
30	4-6-40	B coli Strep Entero	0.5	20 hrs	80 80	S Q	Died 4-11-40	Peritonitis	B coli Entero
31	4-8-40	B coli Diplococci	0.5	12 hrs	None		Died 24 hrs	Peritonitis	B coli Gram positive diplococci
32	4-8-40	B coli Diplococci	0.5	12 hrs	80	I P	Died 24 hrs	Peritonitis	B coli Entero
33	4-8-40	B coli Diplococci	0.5	12 hrs	80	S Q	Died 24 hrs	Peritonitis	B coli Entero
34	4-10-40	B coli Strep.	0.4	16 hrs	None		Died 4-8-40	Localized peritonitis	None
35	4-10-40	B coli Strep.	0.4	16 hrs	80	I P	Lived		
36	4-10-40	B coli Strep	0.4	16 hrs	80	S Q	Lived		
37	4-13-40	B coli Strep	0.5	6 hrs	None		Died 24 hrs		B coli Strep
38	4-13-40	B coli Strep	0.5	6 hrs	40 40 24 hr intervals	I P	Died 4-16-40	Peritonitis	B coli Strep
39	4-13-40	B coli Strep	0.5	6 hrs	40 40 4 hr interval	S Q	Died 4-18-40 (lived 48 hrs longer than I P)	Marked pleuritic exudate	B coli Strep
40	4-15-40	B coli Diplococci B pyocyaneus	0.5	6 hrs	None		Died 4-16-40	Peritonitis	B coli B pyocyaneus
41	4-15-40	B coli Diplococci B pyocyaneus	0.5	6 hrs	40 40 4 hr intervals	I P	Died 4-19-40 (lived 3 days longer than S Q)	Peritonitis	B coli B pyocyaneus

S Q Subcutaneous

TABLE II.—THE INJECTION OF INTRAPERITONEAL SULFANILAMIDE POWDER AND SULFANILAMIDE SOLUTION IN ADVANCED PERITONITIS OF RATS, DURING PERIOD OF MARCH 23 1940 TO APRIL 23, 1940—Continued

No.	Date	Culture	Amount cc	Duration of peritonitis	Sulfanilamide		Result	Postmortem examination	Postmortem culture
					Amount in mgm.	Route			
43	4-13-40	B coli Diplococci B pyocyaneus		hrs	50 50 12 hr intervals	B Q	Dead 4-26-40	Peritonitis	B coli B pyocyaneus
43	4-16-40	Diplococci B coli B pyocyaneus	0.6	4 hrs	None		Dead 4-17-40	Peritonitis	B coli B pyocyaneus
44	4-15-40	Diplococci B coli B pyocyaneus	0.6	4 hrs	50	I P	Dead 4-17-40	Peritonitis	B coli B pyocyaneus
45	4-15-40	Diplococci B coli B pyocyaneus	4	4 hrs	50	B Q	Dead 4-17-40	Peritonitis	B coli B pyocyaneus
46	4-17-40	B coli Strap.		hrs	None		Dead 4-18-40	Peritonitis local	Strap B coli
47	4-17-40	B coli Strap.	5	hrs	50	I P	Lived		
48	4-17-40	B coli Strap.	5	hrs	50	B Q	Dead 4-18-40		
49	4-18-40	B coli Strap.		hrs	None		Dead 4-19-40	Peritonitis-focal	B coli Strap.
50	4-18-40	B coli Strap.		hrs	50	I P	Dead 4-20-40 Overd 54 hrs (same data B Q)	Peritonitis extensive	B coli Strap.
51	4-18-40	B coli Strap.		hrs	50	B Q	Dead 4-19-40	Peritonitis focal	B coli Strap.
52	4-19-40	B coli Strap.		hrs	None		Dead 4-20-40 (Toxic absorption- time)	Free fluid	coli Strap Saprophytic
53	4-19-40	B coli Strap.		hrs	50	I P	Dead 4-20-40 (Toxic absorp- tion)	Free fluid	B coli Strap Saprophytic
54	4-19-40	B coli Strap.	4	hrs	50	B Q	Dead 4-20-40 (Toxic absorp- tion)	Free fluid	B coli Strap Saprophytic
55	4-21-40	coli Strap.		hrs	None		Dead 4-22-40	Dilatation, dyscalculia	B coli Extens
56	4-21-40	B coli Strap.		hrs	50 4-22-40 50 4-23-40	I P	Dead 4-22-40 (24 hrs longer)	Muddy fluid, some exudate	B coli Extens
57	4-22-40	B coli Strap.	5 hrs		50 4-22-40	B Q	Dead 4-23-40	Much fluid	B coli Extens
58	4-22-40	B coli Strap.		hrs	50 4-23-40 50 4-23-40 4-24-40	I P	Living		
59	4-22-40	B coli Strap.	0.5	hrs	50 4-22-40	B Q	Dead 4-23-40	Much fluid	coli Extens
60	4-22-40	B coli Strap.	0.	hrs	50 4-22-40 50 4-23-40 4-24-40	I P	Dead 4-24-40 (4 days longer)	Peritonitis extensive	B coli Extens
	4-22-40	coli Strap.		hrs	50 4-22-40	B Q	Dead 4-23-40	Much fluid	B coli Extens
	4-23-40	coli Strap.	25	11 hrs	None		Dead 4-24-40	Free fluid	B coli Strap.
63	4-23-40	B coli Strap.	25	hrs	50	I P	Dead 4-24-40	Free fluid	B coli Strap.
64	4-23-40	B coli Strap.	25	hrs	50	B Q	Dead 4-24-40	Free fluid	B coli Strap.
64	4-26-40	B coli Strap.		hrs	None		Dead 4-26-40	Peritonitis	B coli Strap.

B Q subcutaneous

TABLE II—THE INJECTION OF INTRAPERITONEAL SULFANILAMIDE POWDER AND SULFANILAMIDE SOLUTION IN ADVANCED PERITONITIS OF RATS, DURING PERIOD OF MARCH 23, 1940 TO APRIL 28, 1940—Continued

No	Date	Culture	Amount c cm	Duration of peritonitis	Sulfanilamide		Result	Postmortem examination	Postmortem culture
					Amount in mgm	Route			
66	4-26-40	B coli Strep	0.5	5 hrs	75 4-26-40	I. P.	Living		
67	4-26-40	B coli Strep	0.5	5 hrs	75 4-26-40	S Q	Living		
68	4-28-40	B coli Strep	0.5	6 hrs	None		Died 4-29-40	Peritonitis	B coli Strep
69	4-28-40	B coli Strep	0.5	6 hrs	80	I. P.	Died 4-29-40	Peritonitis	B coli Strep
70	4-28-40	B coli Strep	0.5	6 hrs	80	S Q	Died 4-29-40	Peritonitis	B coli Strep

S Q subcutaneous

should be stressed that a peritonitis of 4 to 20 hours' duration in a rat of 150 to 200 grams is comparable in severity to one of days in a human being. It also should be emphasized that many of these rats were already extremely ill when the sulfanilamide was introduced. Occasionally an untoward result occurred, such as an unprotected rat living while the rat with sulfanilamide died. We cannot always explain such results. The variation in individual rats and susceptibility to dosage of sulfanilamide probably are factors. These results are tabulated in Table II.

In this experiment the ability to save the treated rats was not as great as we would have liked. However, of a possible 24 rats protected with intraperitoneal sulfanilamide, there were 17 good results (10 of the rats lived indefinitely). More detailed treatment would probably have been even more productive of good results. The subcutaneous route showed some degree of curative value also, but not to the same extent as the intraperitoneal route. In this phase of the experiment, of 24 rats protected with subcutaneous sulfanilamide there were 7 good results (5 of which lived indefinitely). In the control rats, of 22, 1 rat lived. These results are shown in Graph 2. It should be re-emphasized that this was a rather rigorous experiment, peritonitis had already set in for a varying number of hours and the animals were already quite sick when they were treated.

In summarizing experiment 2 the general effectiveness of sulfanilamide can be shown (Graph 3). Thus of 48 rats given sulfanila-

midate either intraperitoneally or subcutaneously from 4 to 20 hours after peritonitis had set in there were 24 good results.

The final estimate of this therapeutic measure rests with its trial in human patients who have fallen victim to diffuse peritonitis. We must reiterate that our experience has been very small. There have been in all only 4 cases of widely different variety in which it has been utilized. None of these cases necessarily proves anything with the exception of the fact that sulfanilamide which is introduced intraperitoneally is in no way locally destructive or harmful to delicate tissue such as the serosa of bowel.

#### SUMMARY AND CONCLUSION

Most of the papers which have been written to date have emphasized the use of sulfanilamide in a systemic manner. The main purpose of this work is to show that sulfanilamide acts locally even though indirectly in some fashion which is not yet clear. If sulfanilamide can be applied to a local area and kept in contact with this area, it is taken up by the tissues and permeates them thoroughly. This is evidenced by its detection in the blood in very appreciable quantities following intraperitoneal implantation in humans. Traces can even be detected in the blood stream following local application to a granulating wound such as a varicose ulcer. We have demonstrated this fact in human beings to our complete satisfaction.

We feel that the peritoneum is an ideal site for the local use of sulfanilamide. At opera-

TABLE II.—THE INJECTION OF INTRAPERITONEAL SULFANILAMIDE POWDER AND SULFANILAMIDE SOLUTION IN ADVANCED PERITONITIS OF RATS, DURING PERIOD OF MARCH 23, 1940 TO APRIL 23, 1940—Continued

No.	Date	Culture	Amount cc.	Duration of peritonitis	Sulfanilamide		Result	Postmortem examination	Postmortem culture
					Amount in mgm.	Route			
42	4-17-40	B. coli Displaced B. pyocyaneus	1	4 hrs.	50 50 50 by 1 hr. intervals	S Q	Dead. 4-18-40	Peritonitis	B. coli B. pyocyaneus
43	4-17-40	Displaced B. coli B. pyocyaneus	4	4 hrs.	None		Dead. 4-17-40	Peritonitis	B. coli B. pyocyaneus
44	4-17-40	Displaced B. coli B. pyocyaneus	0.5	4 hrs.	50	I P	Dead. 4-17-40	Peritonitis	B. coli B. pyocyaneus
5	4-17-40	Displaced B. coli B. pyocyaneus	0.5	4 hrs.	50	S Q	Dead. 4-17-40	Peritonitis	B. coli B. pyocyaneus
46	4-17-40	B. coli Stryp.	0.5	hrs.	None		Dead. 4-18-40	Peritonitis local	Stryp. B. coli
47	4-17-40	B. coli Stryp.	0.5	hrs.	50	I P	Lived		
48	4-17-40	B. coli Stryp.	0.5	hrs.	50	S Q	Dead. 4-18-40		
49	4-17-40	B. coli Stryp.		hrs.	None		Dead. 4-18-40	Peritonitis-focal	B. coli Stryp.
50	4-18-40	B. coli Stryp.		hrs.	70	I P	Dead. 4-20-40 (Oval 44 hrs. latter (liver S. Q.))	Peritonitis moderate	B. coli Stryp.
51	4-18-40	B. coli Stryp.		hrs.	50	S Q	Dead. 4-19-40	Peritonitis focal	B. coli Stryp.
52	4-19-40	B. coli Stryp.		hrs.	None		Dead. 4-20-40 (liver sloughy- tous)	Free fluid	B. coli Stryp. Saprophytic
53	4-19-40	B. coli Stryp.		hrs.	50	I P	Dead. 4-20-40 (liver sloughy- tous)	Free fluid	B. coli Stryp. Saprophytic
54	4-19-40	B. coli Stryp.	0.	hrs.	50	S Q	Dead. 4-20-40 (liver sloughy- tous)	Free fluid	B. coli Stryp. Saprophytic
55	4-19-40	B. coli Stryp.	0.	hrs.	None		Dead. 4-20-40	Edematous, discoloration	B. coli Enter.
56	4-19-40	B. coli Stryp.		1 hrs.	50 4-19-40 50 4-19-40	I P	Dead. 4-20-40 (44 hrs. longer)	Muddy fluid, some necrosis	B. coli Enter.
57	4-19-40	B. coli Stryp.		hrs.	50 4-19-40	S Q	Dead. 4-22-40	Black fluid	B. coli Enter.
58	4-19-40	B. coli Stryp.		hrs.	50 4-19-40 50 4-19-40 50 4-19-40	I P	Dead. 4-20-40 (4 days longer)	Peritonitis moderate	B. coli Enter.
59	4-19-40	B. coli Stryp.	0.	hrs.	50 4-19-40	S Q	Dead. 4-22-40	Black fluid	B. coli Enter.
60	4-19-40	B. coli Stryp.		hrs.	50 4-19-40 50 4-19-40 50 4-19-40	I P	Dead. 4-20-40	Peritonitis moderate	B. coli Enter.
61	4-19-40	B. coli Stryp.	1	hrs.	50 4-19-40	S Q	Dead. 4-22-40	Black fluid	B. coli Enter.
	4-19-40	B. coli Stryp.	15	hrs.	None		Dead. 4-22-40	Free fluid	B. coli Stryp.
	4-19-40	B. coli Stryp.	15	hrs.	50	I P	Dead. 4-22-40	Free fluid	B. coli Stryp.
62	4-19-40	B. coli Stryp.	0.15	hrs.	50	S Q	Dead. 4-22-40	Free fluid	B. coli Stryp.
63	4-20-40	B. coli Stryp.		hrs.	None		Dead. 4-20-40	Peritonitis	B. coli Stryp.

admit defeat Sulfanilamide given intraperitoneally and subcutaneously in adequate dosage gives the surgeon a positive weapon with which to fight this insidious infection and with which to meet it on perhaps slightly more equal terms

CASE 1 M P, aged 8½ years, female, was admitted to the hospital February 24, 1940, operation was done February 24, 1940, and she was discharged April 1, 1940 Patient gave a history of abdominal pain which had been present 3 days

Physical examination showed a very sick child with abdomen generally distended, rigid, and tender Peristalsis was absent Temperature was 103.6 degrees, pulse, 160, respirations, 35 The white blood cells numbered 50,153, polymorphonuclears, 93 per cent, lymphocytes, 3 per cent, large mononuclears, 4 per cent

At operation there was found a diffuse purulent peritonitis The appendix, perforated and pointing up under the liver, was removed, Penrose drains were inserted, and 15 grains of sulfanilamide was placed in the peritoneal cavity before closure Culture from the peritoneal cavity showed the *Bacillus coli* and the streptococcus

Convalescence was stormy and patient was given 4 grams of sulfanilamide daily in 24 hour periods for 7 days

Following this she was given sulfanilamide by mouth 1-1.0 grains three times a day for 2 days On discharge the wound was healed and there was no evidence of residual abscesses

CASE 2 M R, aged 45 years, female, was admitted to the hospital, April 24, 1940, operation was done April 26, 1940 In hospital at present May 24, 1940

In the past 10 years patient had 5 laparotomies for pelvic disease The last one, one year before admission, was performed to relieve intestinal obstruction Patient had partial intestinal obstruction when admitted After Wangenstein drainage and intravenous glucose, laparotomy was performed The bowel was so thinned out and adhesions so firm that the bowel was opened in 3 places There was gross contamination The obstruction was relieved and an ileostomy was performed Sixty grains of sulfanilamide were placed in the peritoneal cavity before closure Peritoneal culture showed *Bacillus coli*, streptococcus, Gram positive diplococci, Gram positive bacilli Blood sulfanilamide taken the following day showed 5.7 milligrams per 100 cubic centimeters She was subsequently given sulfanilamide subcutaneously in addition

There was little temperature rise and convalescence has been remarkably smooth, except for the ileostomy opening which has not yet closed

CASE 3 Dr M M, aged 26 years, male, was admitted to the hospital May 20, 1940, operation was performed May 20, 1940, and he is at present convalescing

Patient had an appendiceal abscess drained 3 months previously and a persistent fistula remained Several hours before admission patient had abdominal pain with emesis, rise in temperature to 102 degrees, pulse 140 A diagnosis of intestinal obstruction was made The white blood cells numbered 18,200, polymorphonuclears, 84 per cent, lymphocytes, 15 per cent, and mononuclears, 1 per cent Sedimentation time was 19 minutes

At operation the free peritoneal cavity was entered into, the obstruction was relieved, and a pus pocket encountered Gross contamination was present The terminal ileum was suggestive of regional enteritis The appendix appeared to be involved in an acute process and was removed The fistulous tract was cut across Forty-five grains of sulfanilamide was introduced before the wound was closed The abdomen was closed with drainage

Culture from the peritoneal cavity showed *Bacillus coli*, streptococci, and Gram positive diplococci

Convalescence was uneventful and on the third day after operation, the temperature reached normal Forty-eight hours after operation the blood sulfanilamide determination showed a trace present

CASE 4 W A, aged 43 years, was admitted to the hospital, March 13, 1940, operation was performed March 13, 1940, and patient was discharged March 26, 1940 Diagnosis acute gangrenous appendicitis Patient gave a history of 36 hours of generalized abdominal pain localizing in the right lower quadrant, for which castor oil, epsom salts, and ex-lax were taken Vomiting occurred twice

Physical examination revealed generalized abdominal tenderness, rebound tenderness and rigidity, moderate distention peristalsis, absent The temperature was 100.8 degrees, pulse, 100, respirations, 20 Urine was negative on analysis The white blood cells numbered 16,300, polymorphonuclears, 94 per cent, lymphocytes, 6 per cent

At operation the peritoneal cavity was found to be filled with milky fluid, which had some odor No gross perforation was noted, but the appendix was gangrenous and was covered with exudate The bowels were diffusely reddened Culture was taken

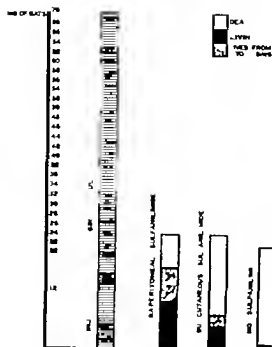
The appendix was removed and 15 grains of powdered sulfanilamide was inserted into the peritoneal cavity at the site of appendectomy One Penrose drain was utilized The peritoneal swab was allowed to dry and was not planted until the next day The final report was no growth Blood sulfanilamide was 24 hours after, 1 milligram per 100 cubic centimeters, 48 hours after, faint trace

The patient had an uneventful convalescence and was discharged on the thirteenth day

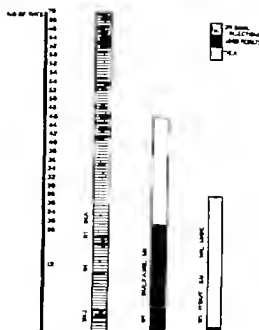
We feel that this patient had peritoneal contamination but the swab was permitted to dry before planting and thus the laboratory proof is lacking

Thanks are extended to Dr H Frankenstein for the use of his cases, to Dr K Yarduman, pathologist, for his intimate advice and co-operation, and to Miss Rhea Klein for her bacteriological studies





Graph 1. Experiment 1.



Graph 2. Summary of Experiment 1.

tion, if one encounters a diffuse peritonitis, sulfanilamide powder in the dosage of 1 to 4 grams can be placed in the peritoneal cavity after removal of the focus and before closure is carried out.

Our experiments with rats although by no means conclusive show some degree of protection afforded by intraperitoneal implantation of sulfanilamide. The first experiment in no way settles the contention that the beneficial effect of sulfanilamide was due to its local effect although we lean to this explanation. However more experiments are being conducted to prove this point. The second experiment tends to confirm in a small way that intraperitoneal sulfanilamide has some advantage over the parenteral method suggesting that the action is more than that of absorption and systemic action, and probably due to sulfanilamide action because of increase in the drug concentration at this point. We are sure of one fact, and that is that intraperitoneal sulfanilamide is not irritating to the peritoneum and apparently is not harmful to the individual. We feel it is advantageous to be able to obtain a high concentration of sulfanilamide

in the peritoneal cavity at the time of and immediately following operation. We must emphasize that in the human being one cannot depend on the one instillation of intraperitoneal sulfanilamide. This must be immediately augmented by subcutaneous sulfanilamide. Ravdin has shown a remarkably low mortality rate in the treatment of all types of acute appendicitis since the subcutaneous use of sulfanilamide has been introduced. We feel that this is a definite forward step in the treatment of peritonitis. It is our opinion that the introduction of powdered sulfanilamide into the peritoneal cavity at operation after the removal of the offending focus will result in an even lower mortality rate. This procedure is not offered as any substitute for time honored and well established methods which are utilized in the treatment of peritonitis, but merely as an additional weapon in the constant struggle against this dread disease.

Many times we have stood by the bedside feeling terribly helpless in the presence of a slowly advancing diffuse peritonitis, hoping against hope that nature's defenses would be able to stem this awful invader. Too many times the invader has won and we have had to



Since submitting this paper we have had 6 cases of generalized peritonitis secondary to perforated appendices in which intraperitoneal sulfanilamide was used. All of these cases have recovered.

## REFERENCES

1. COLLIERBOOK, BUTLER, and O'MARA. *Lancet*, 936, 2 573.
2. COLLIERBOOK and KIRBY. *Lancet*, 936, 2 797.
3. DOMANT. *Deutsche med. Wochenschr.* 936, 5 6 570.

4. LEVADEN and VAREMAN. *Compt. rend. Soc. de biol.* 936, 809.
5. LOCKWOOD, J. S. *Ann. Surg.* 936, 68 802.
6. Idem. *J. Am. M. Ass.*, 940, 114-935.
7. LONG and BURR. *J. Am. M. Ass.* 937 708 31.
8. Idem. *J. Am. M. Ass.*, 937, 99: 544.
9. MARSHALL, ECKHORN, and CUTTING. *J. Am. M. Ass.*, 937 68 913.
10. RAYSON, RHODES, and LOCKWOOD. *Ann. Surg.* 940, 53.

## THE TREATMENT OF ACUTE APPENDICITIS IN A MUNICIPAL HOSPITAL

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**A**s a rule, the patient undergoing treatment in the average municipal hospital is in a more advanced stage of disease at the time of his hospital admission, and, as he is from the so called "under-privileged" group is usually in less satisfactory physical condition at the onset of his disease. For these reasons, we felt it worth-while to report the results of the treatment of acute appendicitis in the period 1935-1940 at the Edward J. Meyer Memorial Hospital. This hospital is operated by the City of Buffalo and is a general hospital of 1 063 beds. The patients, in the vast majority receive some form of city or county aid. Patients paying their own hospital bills constitute not more than 5 per cent of the patient total. Therapy was carried out by the attending or by the resident staff under the direct supervision of the attending staff so that the study represents the work of a fairly large group of surgeons. The basic therapy and operative technique however did not vary significantly during the period of this study. Radical therapy was carried out except in a few instances in which the condition of the patient did not permit it. Frank appendiceal abscesses were also treated conservatively until an optimum time for operation was reached. During this period 527 patients

with acute appendicitis have been treated. In this study no case was accepted as one of acute appendicitis without confirmation by the pathologist, except those cases of appendiceal abscess in which the appendix was not removed.

### ACUTE NONPERFORATED APPENDICITIS

Three hundred and forty cases of acute nonperforated appendicitis were treated during this period, with 2 deaths, or a mortality rate of 0.58 per cent. Both of these deaths occurred during the first year of this study. One of these patients suffered a pulmonary embolism on his seventh postoperative day his second day out of bed. The other a child was suffering from measles at the time of the appendicitis attack, and died on the fourth postoperative day with a clinical diagnosis of generalized peritonitis.

In this group surgery was carried out immediately following admission and diagnosis, except in a few instances wherein replenishment of fluid loss was considered advisable. The operation was performed in all cases within 12 hours of hospital admission. With rare exceptions the McBurney incision was used with or without the Weir extension. Gas and ether anesthesia was used in 318 cases, spinal anesthesia in 18 and local anesthesia in 4 cases. Both deaths occurred in the first group. Morphine was given after operation as needed. Fluid requirements were met by oral ad

In the cases compiled from the literature (1) a total of 4,344 were perforated, or 20.96 per cent of the acute cases. In our series 187 cases were perforated, or 35.4 per cent of the total. This would seem to indicate that appendicitis is seen in graver form in the municipal hospital. The usual causes of procrastination and purgation are, as usual, responsible.

## BIBLIOGRAPHY

- 1 BANCROFT, F. W., and SKOLUDA, E. R. Appendicitis. Study of 596 consecutive cases. *New York J Med*, 1936, 36: 507-509.
- 2 BUNCH, G. H., and DOUGHTY, R. Treatment of acute appendicitis. *Ann Surg*, 1937, 106: 42-48.
- 3 DE COURCY, J. L. Care of the ruptured appendix, reduction of mortality to four per cent in a series of fifty cases. *Surg, Gynec & Obst*, 1936, 63: 756-760.
- 4 GARLOCK, JOHN H. Acute appendicitis, controllable mortality factors. *Am J Surg*, 1934, 23: 248-254.
- 5 HOLDER, H. G., and WELLS, J. T. Survey of appendicitis in San Diego. *Surg, Gynec. & Obst*, 1937, 64: 239-244.
- 6 KEYES, E. L. Deaths from appendicitis. Mortality from appendicitis and causes of death following appendicitis. *Ann Surg*, 1934, 99: 47-68.
- 7 RAY, B. S. Study of appendicitis—1500 cases at New York Hospital. *New York State J Med*, 1938, 38: 412-423.
- 8 REIM, M. R., POER, D. H., and MERRELL, P. Statistical study of 2,921 case of appendicitis. *J Am M Ass*, 1936, 106: 665.
- 9 SCHULLINGER, R. M. Acute appendicitis and associated lesions, some observations on mortality. *Arch Surg*, 1936, 32: 65-98.
- 10 SPRAGUE, E. W. et al. Study of appendicitis, analysis of 1463 consecutive cases. *Surg, Gynec & Obst*, 1938, 66: 166-172.
- 11 STRAUSS, A., and TOMARKIN, J. Acute appendicitis. *Surgery*, 1938, 3: 111-120.
- 12 TOTTEN, H. P. Mortality factors in appendicitis with perforation. *Ann Surg*, 1937, 106: 1035-1045.

Perforation with localized peritonitis occurred in 44 cases. Of these 39 recovered and 5 died, a mortality of 11.3 per cent. The causes of death were (1) generalized peritonitis in 4 cases—autopsy, (2) localized peritonitis with massive intra abdominal hemorrhage 1 case—confirmed at autopsy. Drainage was used in 24 cases, with 3 deaths, a mortality of 12.5 per cent. No drainage was used in 16 cases 1 death occurred or a 6.3 per cent mortality.

In these cases it is more difficult to assay the rôle of drainage as it was usually employed in the presence of small collections of pus or necrotic material.

In résumé as to perforation with peritonitis, there was a total of 127 cases with 18 deaths or a 14.1 per cent mortality.

#### PERFORATION WITH ABSCESS FORMATION

Our treatment of perforation with abscess formation (the presence of a mass at the time of admission) has been definitely conservative. Patients were not operated upon until their general condition was satisfactory and it was evident that the abscess wall was sufficiently firm to permit its incision without risk of further peritoneal contamination. Limitation of fluids by mouth and parenteral fluid administration together with adequate doses of morphine were employed according to the condition of the patient. Here again, blood transfusions have been used with increasing frequency. Drainage has been carried out as an extraperitoneal procedure either through the abdominal wall, rectum, or vagina, as the occasion has indicated. The detailed treatment of the appendiceal and postappendiceal abscess will be discussed in a later paper. The appendix is removed at the time of drainage only when it is easily accessible and when its removal can be carried out without fear of breaking down the abscess wall. All patients whose appendices had not been removed were informed of this and requested to return in 8 to 12 weeks for appendectomy.

Abscess was present in 57 cases. Of these 7 died, a mortality of 12 per cent.

The causes of death were (1) Generalized peritonitis—2 cases (no autopsies—appendectomy performed in both instances) (2)

postoperative shock—2 cases (1 boy, aged 4, did not recover from the anesthesia and died 4 hours after operation. The other patient died within the first 24 hours) (3) wound disruption with secondary hemorrhage 7th postoperative day (no autopsy) (4) acute cardiac dilatation induced by insulin shock, sixteenth postoperative day (no autopsy) (5) pulmonary embolism, eleventh day (no autopsy).

As our mortality rate for the treatment of abscess is somewhat higher than the average of the reported series, we are inclined to think that errors in judgment or technique are the responsible factors. Omission of appendectomy might have eliminated the 2 deaths from generalized peritonitis. The 2 "shock" cases may be blamed on poor judgment or technique. If these 4 fatalities had been prevented, the mortality rate would have been quite respectable.

#### NON-OPERATIVE THERAPY

Nine patients with acute appendicitis, presumably with peritonitis, were treated without operation because they were *in extremis* at the time of admission, and at no time were possible operative risks. All of these patients died, but because only 3 had postmortem examinations these 3 alone were considered as proved cases of appendicitis.

#### SUMMARY

In a 5 year period 1935-1940, 527 patients with acute appendicitis were treated at the Edward J. Meyer Memorial Hospital. These cases have been subdivided as acute non-perforated, acute perforated with generalized or localized peritonitis, acute perforated with abscess. The results compared with those found in the recent literature are shown briefly in Table I.

TABLE I

	Cases	Mortality Per cent
Literature (gross total)	2284	4.66
Edw. J. Meyer Memorial Hospital	377	5.3
Perforation—no peritonitis		
Literature	8009	26.11
Edw. J. Meyer Memorial Hospital	37	14.17
Perforation with abscess		
Literature	8093	10.12
Edw. J. Meyer Memorial Hospital	57	

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Nichols (19), in March, 1899, reported a case in which he observed thickening of the skin, absence of fatty tissue and adherence of the dense, fibrous bands to the skin Elsewhere the epidermis, dermis, and subcutaneous tissue were normal He noted an increased proliferation of connective tissue cells in and about the blood vessels, some fasciculi of the fascial bands were composed mainly of cells The sweat glands were numerous and unchanged In October, 1899, the same author (20) in another paper reviewed the literature and presented the results of microscopic study in 2 other cases In the first of these, the palmar fascia was thickened and the process involved the skin He noted particularly the absence of sweat glands in the involved skin and increased thickness of the stratum corneum The palmar fascia was made up of dense fasciculi of white fibrous tissue Toward the wrist this band was acellular and avascular but in other places there was marked proliferation of connective tissue cells and capillaries In the second case the palmar fascia was merely one dense fibrous band which contained numerous nuclei, but few blood vessels This writer described the lesion as essentially a hypertrophy of connective tissue He stated that during an early or developing period the cellular or vascular elements occur in great abundance but at a later stage when the lesion is fully developed and stationary, the cells and vessels diminish leaving the abnormal tissue, a dense mass of connective tissue which is similar to the pre-existing normal palmar fascia

In 1897, Anderson considered the condition to be inflammatory hyperplasia or neoplastic growth which began in the skin and subcutaneous tissues of the palm and by a process of nuclear proliferation spread along the course of the blood vessels, replacing the adipose tissue and, secondarily, involving the palmar fascia Ledderhose (13), in 1897, described a similar pathological condition in the plantar fascia, which he termed "plantar fasciitis" In another article on palmar fasciitis in 1920, the

same author (14) ascribed Dupuytren's contracture to a chronic proliferative process without inflammation

In 1902, Janssen studied the microscopic anatomy of the hand in 7 cases and gave a comprehensive description of his observations He noted the early thickening of the palmar fascia, then the formation of small knots, and finally, the contracture of the fascia and adherence of the skin to the fascia On microscopic examination he described the process as a proliferation of fibrous tissue from multiple foci which extended down to, and involved, the tendon sheaths He described the close resemblance microscopically between the cellular fibrous tissue and fibrosarcoma, he even noted the occasional presence of mitotic figures He concluded, however, that Dupuytren's contracture is not a neoplastic process nor an inflammatory process as there are no signs of inflammation and the lesion is purely a hypertrophic process

In 1918, Coenen made a complete and detailed review of the literature and concluded that Dupuytren's contracture is chronic inflammation of the superficial palmar aponeurosis with vascularization and proliferation of new cells He did not report any studies or observations on cases of his own

In 1920 and 1921, Krogus (11, 12), from observations on his own patients, made a distinction between new and old cases In the new cases, newly formed connective tissue appeared, in the old cases, the bands were hard, strong, and hyalinized He ascribed the contracture to the proliferation of embryonic rests of primitive muscles of the palm—the flexores breves manus superficiales

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## THE ETIOLOGY AND PATHOLOGY OF DUPUYTREN'S CONTRACTURE

HENRY W MEYERDING M.D., F.A.C.S JOHN R. BLACK, M.D. and  
ALBERT C. BRODERS, M.D. Rochester Minnesota

THE etiology of Dupuytren's contracture has not been established definitely. In previous publications, one of us (Meyerding 15-18) has reported his clinical, surgical, and postoperative observations. Available tissue removed at operation has been examined microscopically in order to determine the pathological changes. We recognized, as other pathologists have that the thickened and contracted palmar fascia caused the deformity. The fascia in these cases is characterized by definite proliferation of its fibrous components. A search was made for the factors involved in the production of this proliferation and in adjacent palmar tissues, areas of increased vascularity and lymphocytic infiltration were discovered. Although there is evidence that heredity and trauma may play a rôle we believe that the inflammatory reaction noted is of prime importance in the etiology of Dupuytren's contracture.

In 1831 Dupuytren gave his first description of what he termed "*retraction permanente des doigts*" (permanent contracture of the fingers) a condition which has subsequently been named after him. Although Dupuytren was not the first to recognize that the palmar fascia was chiefly responsible for the flexion deformities of the fingers, he described the gross pathological changes so clearly and so well that posterity has seen fit to do him honor by giving his name to this clinical entity. He observed from his dissections that the skin of the palm had small hard knots and wrinkles which disappeared when the skin was dissected from the palmar fascia. The palmar fascia itself was hard and thick, diminished in length, and was under tension. The prolongations from the fascia distally ran to the sides of the proximal phalanges of the fingers. The

contracture of these prolongations of the palmar fascia produced flexion of the fingers. Examination of tendons and joints revealed them to be entirely normal.

The descriptions of the microscopic pathology given by the early authors were meager. In 1877 P. Richer dissected the left hand in a case of bilateral Dupuytren's contracture. He stated that the skin was firmly adherent to the underlying fascia, but was scarcely changed microscopically. The superficial fascia was thickened, hard, and shortened owing to an increase in the number and size of the elastic and collagen fibers. He concluded that the palmar fascia was the only structure altered. No signs of inflammation were noted, but he classified the changes as the same as those in chronic articular rheumatism. In 1882, F. Chevrot made a study of the histological changes in Dupuytren's contracture. He noted the thickened palmar fascia and the absence of the normal adipose tissue separating the fascia from the skin. In addition however he described a thickening of the epidermis, which he attributed to the protection of the surface epithelium from friction as a result of the contracture. He noted a thickening of the lining of the sweat glands.

Langhans, in 1887 apparently made a thorough pathological study of Dupuytren's contracture for many of his contemporaries and later writers have quoted from his work (3, 4, 9, 10, 13). He is credited with the following observations on the pathogenesis of Dupuytren's contracture. It is an inflammatory and proliferative process which begins in the interstitial connective tissue and in the adventitia of the blood vessels. This process involves the palmar fascia and leads to an increase in the number and thickness of the bands of connective tissue. In the fascia the number of nuclei is increased but they also occur in scattered groups throughout the fat and interstitial con-

From the Section on Orthopedic Surgery, the Mayo Clinic and the Mayo Foundation and the Division of Surgical Pathology, the Mayo Clinic.

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More recently other authors (4, 8, 21) have reviewed the literature but few have investigated the microscopic pathology and little has been added to the observations of the earlier writers.

There has been great unanimity of opinion regarding the nature of the pathological changes in the palmar fascia. It becomes hard and thickened and presents varying degrees of cellular proliferation. The descriptions of changes in the other tissues of the palm are far from consistent. Some investigators have noted involvement of the skin and subcutaneous tissue others have not. Many have noted the formation of new connective tissue and blood vessels, but most authors have denied the presence of leucocytes in the affected tissues.

The etiology of Dupuytren's contracture has long been a problem to the medical world. We do not wish to discuss it in detail but wish merely to point out the relationship of the histological changes to the etiology. Dupuytren himself expressed the belief that local trauma played a large part in the production of contracture of the palmar fascia because, in his experience it was more common in manual laborers. Contemporary writers associated contracture of the palmar fascia with gout, but at the same time they confused gout with various forms of arthritis (chronic infectious arthritis, senescent arthritis, and so forth). Many investigators have noted the association of contractures of the fingers with contractures of the palmar fascia following lesions of the central nervous system, such as tabes dorsalis, multiple sclerosis, syringomyelia, and injuries to the spinal cord and also of the peripheral nerves after fractures and other trauma. Heredity has long been known to be an outstanding predisposing factor. Chronic infection has long been a subject of much debate. The chief opposition has been based on the lack of evi-

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#### HISTOLOGY OF THE NORMAL SKIN OF THE PALM AND FASCIA

Before considering the pathological changes which occur in the palm in Dupuytren's contracture we shall review briefly the normal histology. In order better to compare the pathological changes (Fig. 1) The normal skin of the palm has a similar structure to skin of other parts of the body. It differs in certain respects in that it contains no hair follicles or sebaceous glands and deep in the subcutaneous tissue there is a dense layer of fascia, the palmar fascia.

The skin consists of three main layers: the epidermis, the dermis, and the subcutaneous tissue. The epidermis is made up of stratified epithelium in various stages of its growth as the cells grow from the basal layer outward through the prickle-cell stage, then become keratinized and finally are shed as dead scale epithelium.

The dermis, or corium, is that portion of the skin which lies immediately beneath the epidermis and carries the nerves and blood vessels which supply the skin. The dermis is made up of two strata, a deeper reticular layer and a superficial papillary layer. The surface of the papillary layer presents numerous conical elevations, the papillae of the corium which project into the under surface of the epidermis. These papillae are abundant in the palm. They consist of a fine supporting network of connective tissue for the finer branches of the cutaneous blood vessels and nerves. A few wandering cells and lymphocytes may be seen particularly just beneath the basal layer of the epidermis. The deeper portion of the corium consists of interlacing bundles of connective tissue fibers which form a moderately loose network. These bundles are much coarser than those of the papillary layer and seem to pursue a wavy or spiral course. This loose regular arrangement of collagen bundles gives to the reticular layer the appearance of having been braided or woven. It is this loose elastic structure of the derma which allows the skin to stretch and bend with every movement of the hand. The reticular layer contains the

larger blood vessels of the corium and many small nerve trunks. The secreting portion of many of the sweat glands lies in the deeper portion of the reticular layer, most of these glands, however, lie in the superficial layers of the subcutaneous tissue.

The subcutaneous tissue consists of a coarse network of narrow strands of connective tissue, which pass between the reticular layer and the palmar fascia. The meshes of this network are occupied by lobules of adipose tissue. The palmar fascia consists of a thin layer of dense connective tissue. The collagen fibers are straight and are packed close together in parallel bundles. The fascial bands form a sheath of tissue parallel to the surface of the skin and are connected to the skin superficially and to the deeper structures by thin strands of dense, strong connective tissue. The nuclei in the connective tissue of the fascia are few, very small and elongated as they lie between the collagen fibers.

Connecting and filling the spaces between the various layers of the skin, subcutaneous tissue and fascia is a very loose network of connective tissue made up of loose bundles of wavy collagen fibers. It forms the supporting tissue for the blood vessels and nerves as they lie deep to the palmar fascia. The few nuclei of the connective tissue in this interstitial tissue are small and stellate. Only an occasional wandering cell is seen in the normal connective tissue.

#### MATERIAL STUDIED

In 1936, one of us (Meyerding, 16) reported observations made on 448 hands of 273 patients with Dupuytren's contracture. Eighty-four, 31 per cent, of the patients were subjected to operation. The material studied in the present investigation consisted of the available specimens removed at operation in this series of cases as well as others obtained since 1935. Specimens from 57 cases were studied, the cases were encountered in the period from January, 1913, to July, 1938 inclusive. These specimens, in the main, consisted of the contracted palmar fascia, in many cases, the entire fascia, in others, just the contracted bands. In some cases, the overlying skin was removed still attached to the fascia, in many specimens

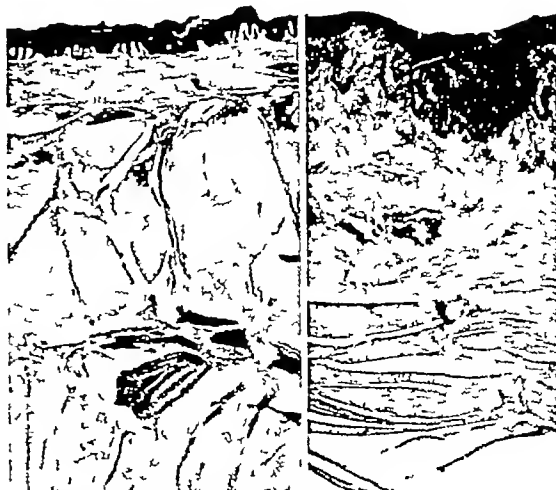


Fig 1, left. Normal skin showing the various layers including the palmar fascia.  $\times 11$ .

Fig 2. Skin in Dupuytren's contracture showing thickening of the epidermis with hyperplasia of all the zones.  $\times 21$ . The normal structure of the corium is completely changed, the papillary layer is distorted and there is a marked perivascular lymphocytic infiltration in all layers, this is most marked in the papillary zone. The regular pattern of the reticular layer is completely disrupted. The subcutaneous tissue has disappeared and the palmar fascia is adherent to the deeper layers of the skin. Sweat glands are entirely absent.

in which all the layers of the skin were lacking, the deeper layers of the skin were present and in these the sweat glands and other structures could be studied. Many of the studies made in the past were incomplete because the specimens available were only small fragments of contracted fascia. Some authors, it is true, studied the entire hand at necropsy, but the number of such cases is small. On the whole, the specimens studied in our series probably represent more complete samples of the palmar fascia and neighboring tissues than those studied by early pathologists. This fact may account for the failure of these men to observe some of the tissue changes which will be described by us in the following paragraphs.

The tissues were fixed in 10 per cent formalin, sectioned with the freezing microtome, and stained with hematoxylin and eosin. Sections were taken from various places on the tissue removed from each patient, in order to select the most characteristic. That is, cross sections and longitudinal sections were made through the fascia and skin including any of the nod-

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Fig. 3.

Fig. 3. Thickened palmar fascia and adherent tissue  $\times 5$ . The fascia shows proliferation grade of new connective tissue cells. Surrounding tissue shows marked fibrosis, new capillaries and perivascular lymphocytic infiltration which is replacing the fatty tissue. Not areas marked X and Y which are shown in detail in Figures 4 and 5.



Fig. 4.

Fig. 4. Chronic inflammatory tissue replacement of fat  $\times 87 \times$ . This photomicrograph represents the area marked X in Figure 3.



Fig. 5.

Fig. 5. Partial destruction of sweat glands and invasion by lymphocytes,  $\times 87 \times$  tissue from area marked Y in Figure 3.

ules that were present. It was often impossible to distinguish in the gross specimen the digital from the carpal fascia.

#### PATHOLOGICAL FEATURES

The descriptions of the pathological changes in Dupuytren's contracture even from the earliest times have emphasized the fibrosis and contracture of the palmar fascia. The changes which were observed in the skin and subcutaneous tissue were regarded as secondary to the contracture of the fascia. Certainly the gross deformity and chief manifestations of the disease are due to contracture of palmar fibrous tissue of which the palmar fascia is the chief constituent.

It is difficult to determine in which tissue or tissues the primary effect takes place because it is only rarely that tissue is obtained in a very early stage of the disease. Recently after the present review had been completed a patient was seen with bilateral plantar fasciitis, the analogue of Dupuytren's contracture in the foot. In this case the plantar fascia presented all the appearances of normal fascia, microscopically. The collagen fibers were closely packed in parallel bundles and were hyalinized. The cells in the connective tissue of the fascia were mature small flat tened and squeezed in between the fibers of the fascia. However in the loose connective and adipose tissue between and around the fascial bundles were numerous new capillaries each of which was surrounded by a large num-

ber of lymphocytes. A specimen of skin was not obtained, but clinically it was unchanged. In early cases of Dupuytren's contracture however the palmar fascia is tightened but even before any contracture takes place the skin becomes thickened and puckered. It is bound down to the underlying tissue and is no longer freely movable. In most instances, we observed that our sections revealed involvement of both the adipose tissue and the palmar fascia. In all cases in which the overlying skin was available for study definite pathological changes were noted in it. It is probable therefore that the disease begins in the interstitial connective tissue and usually spreads to involve all the tissues of the palm down to the deep structures: tendon sheaths, nerves, and blood vessels.

It is a peculiar fact that the disease process should affect the ulnar aspect of the palm more than any other portion. Although the skin, subcutaneous tissue and palmar fascia are affected yet in any one case only portions of the skin or other tissues are involved. Certainly the skin over the thenar eminence and proximal portion of the palm usually is not affected and this also applies to the subcutaneous tissue and palmar fascia.

In 10 cases, portions of skin in the region overlying the contracture were available for study. In others, although the outer layers were absent, frequently the deeper layers of the corium were adherent to the contracted tissue. The layers chiefly affected were the

reticular and papillary zones of the corium and in all the available cases an increase in the number and density of the connective tissue fibers was noted (Fig 2). The reticular zone loses its regular arrangement and loosely woven structure. The fibers, normally running parallel to the surface, become dense masses of connective tissue running in every direction. This accounts for the clinical loss of elasticity of the skin. The papillae of the skin are also changed and become irregular. There is hypertrophy of the epidermis with marked proliferation of all the layers. Numerous new capillaries are seen in the corium surrounded by small groups of lymphocytes. The number of lymphocytes increases in the papillary layer of the corium just beneath the basal layer of the epidermis.

In normal skin the line of demarcation between the dermis and subcutaneous tissue is clearly defined. In this region are found the secreting portions of the sweat glands. In advanced cases of Dupuytren's contracture evidence of subcutaneous adipose tissue is not revealed (Fig 2) and sweat glands are rare or completely absent. Dense parallel strands of fascia lie just beneath and closely adherent to the reticular layer of the dermis. In less advanced cases (Figs 3 and 4) the sweat glands are surrounded by fibrous tissue and numerous lymphocytes, the latter are also seen between the acinar lobules of the gland itself (Fig 5).

The deeper layers of the subcutaneous tissue show an increase in the size and number of the connective tissue bands which normally separate the lobules of fat. There is an increase in the number of capillaries in the interstitial connective tissue and the capillaries are surrounded by lymphocytes. The more advanced the disease the greater is the degree of fibrosis. Infiltration seems to precede the fibrosis (Figs 3, 4, and 5) since the new capillaries and lymphocytes are more numerous about the still unchanged fat cells. The fat appears to be absorbed or destroyed by this process, then new connective tissue forms and obliterates the capillaries and the lymphocytes also disappear. The palmar fascia is separated from the nerves and vessels to the fingers by a layer of adipose tissue. This fatty tissue may also be involved and the thickened

and scarred fascia is closely adherent to the deeper structures. For this reason, nerves and blood vessels were occasionally found embedded in the contracted fascia.

In 24 of the 57 cases, there was definite lymphocytic infiltration of the skin or subcutaneous tissue, only occasionally were plasma cells or polymorphonuclear leucocytes noted. The lymphocytes were commonly found around the sweat glands, blood vessels, and fat cells. The other components of this process, new connective tissue and capillaries were noted in various degrees in most cases and on this basis each case was graded according to the activity of this process.

The palmar fascia gives a picture entirely different from that described in the other tissues, but the changes in this structure are the ones that have been commonly described as characteristic of Dupuytren's contracture. Proliferation of new capillaries and perivascular infiltration of lymphocytes are almost entirely lacking in the palmar fascia itself. Only occasionally are new capillaries seen and in no instance were lymphocytes seen in the fascia. The characteristic change is the proliferation of fibroblasts in the nodules of the contracture. These fibroblasts are round, oval, or spindle-shaped with pale staining nuclei and tend to grow in masses with their long axis, parallel to one another. In very cellular areas (Figs 6, 7, 8, 9, and 10) where the nuclei are closely packed, many mitotic figures may be seen. In this tissue all stages can be demonstrated from those just described to that in which the collagen fibers lie packed together so tightly that the thin, flattened nuclei can scarcely be distinguished (Fig 11), the fibers in such portions of the fascia are frequently hyalinized. The marked cellular proliferation is usually seen in the thickened areas of the fascia which correspond to the base of the fingers in the palm. As new fibrous tissue is deposited and contracts, the fibrous connective tissue cells become mature and flattened, forming streaks through the fascia as shown in Figure 9.

We have assumed that the cellular nature of the fascia described indicates the activity of the proliferative process and, therefore, the degree of maturity of the connective tissue was graded on a basis of 1 to 4. The least ma-

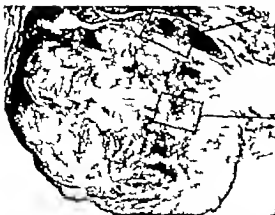


Fig. 6. Nodule from Dupuytren's contracture.  $\times 18$  g. Maturity of connective tissue of palmar fascia in grade 2 there is marked cellularity but the cells are smaller and there are more intercellular fibers than in grade 1. Not partially destroyed fat lobules. Area marked X is shown under high-power magnification in Figure 7 from in Figure 8.

ture process in which the tissue was very cellular was graded 1 (Fig. 12) the most mature in which the nodules were very small and very few in number when compared to the collagen fibers, was graded 4 (Fig. 14). Intermediate

degrees were graded 2 (Figs. 6 and 7) and 3 (Fig. 13).

A specimen of palmar fascia was removed surgically from 63 hands belonging to 57 patients. Sixty-one specimens were studied; the maturity of connective tissue was graded and the degree of the inflammatory reaction was estimated. In all cases the degree of inflammatory reaction was mild. The maturity of connective tissue was grade 1 in 9 cases, grade 2 in 19 cases, grade 3 in 15 cases and grade 4 in 18 cases. The cases studied in this group, therefore, tended to have a mature degree of connective tissue. When the relationship of the duration of the contracture to the degree of maturity of the connective tissue was considered, in the cases of longer duration the degree of maturity tended to be greater but there was a wide variation in individual cases. Little relationship was noted between the age of the patient and the grade of maturity of the fascia. The degree of contracture seems to depend more on the duration of the process than on the grade of maturity. No definite correlation was found between the degree of contracture and grade of maturity of fascia.

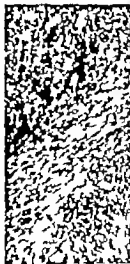


Fig. 7



Fig. 8



Fig. 9



Fig. 10

Fig. 7. Fascia from area marked X in Figure 6.  $\times 3$ . Note the lack of blood vessels, numerous fibroblasts and oval and spindle-shaped nuclei.

Fig. 8. Fat lobule showing blood vessels and large number of lymphocytes replacing fat cells,  $\times 3$  high power magnification of tissue marked Y in Figure 6.

Fig. 9. Fascia with central nodule of very cellular connective tissue.  $\times 30$ . There are also streaks of older nuclei throughout. Area marked Y is shown under higher magnification in Figure 10.

Fig. 10. Cellular nature of tissue from Y in Figure 9. Note mitotic figures.  $\times 75$ .

Recurrence of contracture occurred in 9 cases and when the tissue from these cases was studied it was found that the average grade of maturity for the group was 1 to 2. This represents a much less mature type of connective tissue than in the series as a whole and indicates a more active tissue. On the other hand, a significant increase in the degree of activity of inflammatory changes was not noted.

Occasionally patients with Dupuytren's contracture complain of soreness and tenderness of the affected region although the usual complaints are thickening of the palm, "callus" contracture of a finger or a prickling sensation. It was thought that in cases in which soreness and tenderness of the palm were present greater degrees of inflammatory activity would be found than in other cases. Our studies, however, did not bear this out.

#### COMPARISON OF CLINICAL BEHAVIOR AND PATHOLOGICAL PICTURE

The estimation of the inflammatory reaction and the activity of the proliferation of connective tissue in the fascia, which did not necessarily parallel one another, enabled us to compare the clinical behavior with the pathological picture. One particular conception of Dupuytren's contracture interested us particularly and that was the relationship of the so-called green and mature stages to the prognosis. Our studies bear out the idea that there are various degrees of activity in the process and, in the recurrences noted, the fascia tended to be immature. The number of cases of recurrence studied is too small, however, to state conclusively that in cases in which histological examination reveals a low grade maturity of the fascia recurrence is more likely to occur than in those in which higher grades of maturity are found. In the majority of our cases contractures were well established for they had been present for several years, microscopic examination disclosed in most cases a mature type of connective tissue. Therefore if our theory is correct, it would be natural to assume recurrences to be few in this series.

#### SUMMARY AND CONCLUSIONS

In the past, other investigators have focused their attention on the palmar fascia to the ex-



Fig 11

Fig 12

Fig 13

Fig 11 Palmar fascia, the maturity of the connective tissue is grade 4  $\times 130$ . Hyalinized fascia. The fibers lie closely packed in parallel bundles, the nuclei can scarcely be distinguished. They are few in number, flattened and very small.

Fig 12 Palmar fascia, maturity of connective tissue is grade 1,  $\times 67$ , very cellular fascia with few intercellular collagen fibers. Figures 6 and 7 in which the maturity of the connective tissue is grade 2 should be noted, too.

Fig 13 Palmar fascia, maturity of connective tissue is grade 3  $\times 130$ . Nuclei are smaller and flatter than in Figures 6, 7, and 12 in which the maturity of the connective tissue is graded 2. There is a large amount of intercellular collagen.

clusion of the surrounding tissue and have not described the signs of inflammation, proliferation of capillaries and fibroblasts with marked perivascular lymphocytic infiltration. This inflammatory reaction affects chiefly the skin, subcutaneous tissue, and interstitial connective tissue. The palmar fascia is remarkable for the fact that within its fibers there is evidence of an active proliferation of fibroblasts without other signs of inflammation. The process progresses through the cycle of fibroblastic proliferation, and then deposition of collagen fibers which contract and compress the fibroblasts and the final picture of avascular scar tissue result.

This study further demonstrates the fact that Dupuytren's contracture is not merely a disease of the palmar fascia, but involves all structures from the skin down to the tendon sheaths. It is difficult, therefore, to see how



subcutaneous tenotomy could give consistently good results. On the other hand excision of the mass of scar tissue requires a high degree of surgical skill as emphasized by one of us in a previous paper (17). In cases in which the excised tissue gives evidence of active inflammatory reaction or immature fibrous tissue in the fascia, we believe the likelihood of recurrence is greater.

From the point of view of pathological diagnosis, we wish to point out the danger of confusing Dupuytren's contracture a benign process, with fibrosarcoma. Errors in such a diagnosis have in the past given rise to tragic results. Although certain portions of the tissue removed for Dupuytren's contracture do resemble fibrosarcoma on superficial examination and may even contain numerous mitotic figures, there are many points of difference. Dupuytren's contracture is a diffuse multifocal process; the sarcoma-like areas are located in the palmar fascia at the site of the nodules which are so characteristic of the disease. Surrounding these nodules is dense fibrous tissue. The nuclei are pale staining and regular in shape and size. Local infiltration by these young cells and metastasis do not occur all of which points are against a malignant lesion.

We have studied the microscopic sections of the palmar fascia in 57 cases of Dupuytren's contracture and we have formed the opinion that the pathological picture is best explained on the basis of a chronic inflammatory process.

#### REFERENCES

- ARTHURSON, WILLIAM. Quoted by Nichols, J. B., loc. cit. (9).
- CHENOT, F. Quoted by Nichols, J. B., loc. cit. (9).
- COCHER, H. Die Dupuytren'sche Fingerkontraktur. *Ergebn. d. Chir. u. Orthop.*, 9, 8, 70-96.
- DAVIS, J. S. and FIDELL, H. E. M. Dupuytren's contraction in the note on the incidence of the contraction in diabetes. *Arch. Surg.*, 93, 24, 937-939.
- DEPUYTRE, GUYLAUME. Translation on lesions of the vascular system, diseases of the rectum and other surgical complaints (selections from the collected edition of the clinical papers) by LeGros Clark for the Sydenham Society. 824 pp. 220-220.
- ELKE, OTTO. Zur Histologie und Pathogenese der Dupuytren'schen Kontraktur. *Deutsche Zeitsch. f. Chir.*, 92, 106-121.
- JAKOBSEN, PETER. Zur Lehre von der Dupuytren'schen Fingerkontraktur mit besonderer Berücksichtigung der operativen Beseitigung und der pathologischen Anatomie des Leidens. *Arch. f. Klin. Chir.*, 90, 65, 76-780.
- KAYE, A. B. LUCK, S. L. and MANN, M. I. Dupuytren's contraction with description of the palmar fascia, review of the literature and report of twenty nine surgically treated cases. *Surg. Gynec. & Obst.*, 92, 45, 145-90.
- KIDDER, G. C. Dupuytren contraction of the palmar fascia treated by hypoderm. *Bull. M. J.*, 80, 62-63.
- KOCHER, THEODORE. Behandlung der Retraktion der Palmanneurotome. *Zentralbl. f. Chir.*, 27, 14, 497-503.
- KROGUS, ALL. Neue Gesichtspunkte zur Ätiologie der Dupuytren'schen Fingerkontraktur. *Zentralbl. f. Chir.*, 90, 47, 914-918.
- Idem. Studien und Betrachtungen über die Pathogenese der Dupuytren'schen Fingerkontraktur. *Arch. Chir. Scand.*, 92, 54, 35-50.
- LEONHARDT, ZUR Pathologie der Aponeurose des Fusses und der Hand. *Arch. f. Klin. Chir.*, 27, 55, 604-72.
- Idem. Die Ätiologie der Fasciitis palmaris (Dupuytren'sche Kontraktur). *Muench. med. Wochenschr.*, 92, 14-15.
- MAYNARD, H. W. Dupuytren's contracture. *Proc. Staff Meet. Mayo Clin.*, 93, 10, 602-606.
- Idem. Dupuytren contracture. *Arch. Surg.*, 94, 32, 320-333.
- MAYNARD, H. W. and KROGUS, F. H. Physical therapy in the treatment of Dupuytren contracture. *Physiotherapy Rev.*, 93, 6, 43-45.
- MAYNARD, H. W. and OLIVER, L. M. Bistrial Dupuytren's contracture. *Proc. Staff Meet. Mayo Clin.*, 93, 807-809.
- NICHOLS, J. B. A clinical study of Dupuytren's contraction of the palmar and digital fascia. *Am. J. M. Sc.*, 89, 7, 385-395.
- Idem. The histology of Dupuytren's contraction of the palmar fascia: report of microscopic examination in two additional cases. *Med. News*, 89, 75-79.
- POWERS, HALL. Dupuytren contracture one hundred years after Dupuytren: its interpretation. *J. Nerv. & Ment. Dis.*, 93, 80, 386-400.
- RICHIE, P. Rétraction de l'aponeurose palmaire. *Bull. Soc. anat. de Par.*, 87, 3, 4, 24-29.

# TERATOMA TESTIS

## Survey of Thirty-seven Autopsy Records

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**T**ERATOMA testis is unique among all malignant tumors of the body in that a majority of teratomas have an absolute x-radiation sensitivity. That is, the primary tumors and their metastases have often regressed under external irradiation, and this regression has been permanent. We have had at the Memorial Hospital approximately 600 cases of teratoma testis. By means of high voltage roentgen therapy we have been able to double the cures of this highly malignant disease. At present our 5 year controls are 30 per cent.

Obviously there is much room for improvement.

We have been able to eliminate entirely the one major operation with its attendant mortality, the Chevassu-Hinman dissection of the retroperitoneal tissues with their lymph vessels and glands, which lie along the course of the spermatic vessels. Such a dissection is superfluous if there are no metastases present, and if they already exist then the procedure is inadequate. Deep roentgen therapy is far more efficient. The reasons for this inadequacy lie in the size of the metastases and the frequency with which crossed abdominal metastases occur.

The paucity of postmortem studies of teratoma testis is difficult of explanation. In order better to understand the course of this lesion when uncontrolled, this survey of autopsy material was made. The majority of cases in this series has had either surgical or irradiation treatment. However, therapy as applied to these cases is not the consideration of this review. The survey has been of vast importance in indicating a rational therapy for the future.

**Age** The youngest patient was 9 months old—the oldest patient was 47 years, with an

average age of 31.5 years. Only 36 cases were used in calculating the average age because one patient was a premature stillborn of 8 months.

**Trauma** A history of trauma preceded the patient's observation of testicular enlargement in 6 cases. But the instances are woefully inadequate as to the exact site of the trauma, the appearance of the testicle, ecchymosis, swelling, etc., immediately following the trauma, and the sequence of events between the trauma and the appearance of the teratoma. We are quite sure we have never seen a case in which we have believed that there was even reasonably proved a connection between trauma and the causation of the teratoma.

**Various types of teratoma testis** There were 10 cases, 27.0 per cent, of embryonal carcinoma with lymphoid stroma, 9 cases, 24.3 per cent, of embryonal carcinoma. These two classes comprising half of the cases are most radiosensitive.

There were 10 cases, 27.0 per cent, of embryonal adenocarcinoma, less sensitive to irradiation.

One case, 2.7 per cent, of teratomatous adenocystoma (adult teratoma), still less radiosensitive.

Three cases, 8.2 per cent, of chorionepithelioma, the least radiosensitive of all.

Four cases, 10.8 per cent, unclassified.

**Site involved and cryptorchidism** The right testicle was involved 19 times, 51.45 per cent, the left testicle 18 times, 48.55 per cent. Abdominal cryptorchidism with teratoma occurred 4 times 10.8 per cent. Three of these abdominal testicles were unilateral with a teratoma of the retained testicle. One of these was in a stillborn child with no microscopic diagnosis. In one case there was bilateral cryptorchidism with teratoma on one side.

**Aschheim-Zondek reaction** This determination was made in 21 cases. It was positive in 18 cases, 85.7 per cent questionable in 1 case, and negative in 2 cases. Because of the various and inadequate methods used in determining the Aschheim-Zondek tests in the above cases these 85 per cent positive tests are probably not at all accurate. Drs. Dean and Temple, in a recent unpublished review of the Aschheim-Zondek test as applied to teratoma testis cases in the Memorial Hospital came to the following conclusions:

1 The test is inadequate as it has been done because at least 5 mice should be used per level.

2 The test cannot be used to determine the histological type, because there is no close correlation between the hormone level and the type. (Some cases show close correlation but many others show wide discrepancies.) The adult type when purely adult apparently shows a low level. The chorioncarcinomas are consistently high. The great majority of the embryonal carcinomas show levels below 1500 mouse units per liter. The embryonal adenocarcinomas show a complete range of levels from very low to very high.

3 The chief difficulty in attempting to study correlation between the histological type and the hormone level is that a large number of the tumors are mixed and complex. Therefore serial sections should be used in a study of this type. All types may be found in the same tumor thus complicating any attempt at correlation. A new classification is in order: such a new classification is obviously difficult to make.

4. The test is of definite value in predicting the prognosis, because in general, those with high levels die much sooner than those with low levels. Discrepancies are found, and therefore only general statements can be made. Because of the value in predicting prognosis, we believe the test should be made routinely.

5 Our study did not take into complete account the relation of prolans A and B. In the early years of the test, the erroneous assumption that a 1:5 ratio always existed between A and B was followed. This was advanced by Zondek. It seems in all probability

that the determination of prolans B is of more value than it has previously been suspected, and it probably always means a comparatively early fatal outcome. Further work must be done on this.

6 We believe, after an analysis of 203 cases, that values between 0 and 500 have the same significance.

**Gynecomastia** Gynecomastia was noted in 2 cases: 1 unilateral with secretion, 1 bilateral without secretion. In the unilateral case the histological diagnosis was fibrous mastitis. Both cases had positive reactions to the Aschheim-Zondek test.

**Metastases** Metastases from teratoma testis occur through both blood and lymph channels. In a very large percentage of our autopsy cases the metastases were by means of both channels.

**Blood stream metastases** This is through the spermatic artery to the renal artery or aorta and thence to the heart and lungs. Chorionepithelioma may metastasize entirely through the blood stream.

The history of a patient with chorionepithelioma seen at the Memorial Hospital last year demonstrates this.

B V, aged 30 years was admitted to the Memorial Hospital, on July 20, 1930, with the following history: Two months before swelling of the left testicle occurred. One month prior to admission left orchidectomy was done. The diagnosis was chorionepithelioma of the testicle (corroborated in Memorial Hospital). The roentgenological report follows:

S. Submitted films of the chest reveal three rounded bonylike densities, measuring approximately one half inch in diameter in the right lower lung field, suggesting metastatic process. These densities are noted in the films dated June 30, 1930, and July 1, 1930. S. Submitted films of the dorsal vertebrae: lumbar vertebrae, pelvis, including greater portion of the upper shaft of the femora and skull, reveal no evidence of bone metastasis. N. adenopathy in neck. N. abdominal masses. Liver not palpable. Aschheim-Zondek test July 1, 1930. Between 100 and 500 units prolans A per liter and August 12, 1930. 500 A and .00 B. Chest and liver radiated as follows: From six portals of entry—right upper chest anterior and posterior, right lower chest anterior and posterior and liver anterior and posterior—550 r daily at 50 cm. until he received approximately 2150 r each area. Roentgenological examination of chest shows only the faintest suggestion of the upper of three previously discovered nodules in right chest.

*Lymphatic metastases* Ronviere<sup>1</sup> describes the lymphatics draining the testicle as follows

"All lymph trunks of the testicle eventually arrive at the posterior superior border of the organ and thence along the blood vessels of the spermatic cord

"The lymphatics accompany the internal spermatic artery and vein, and having arrived at the point at which these blood vessels cross the ureter, the testicular collecting trunks commence to separate from the spermatic blood vessels. They finally are drained by the abdomino-aortic nodes which run from the level of the renal vein to the bifurcation of the aorta

"The abdomino-aortic nodes are not the sole direct recipients of the lymphatics of the testicle. There are other lymph vessels that terminate in an external iliac node placed on the external iliac vein in front of the point where the latter is crossed by the ureter (The above applies to the testicle proper)

"The lymphatics of the epididymis terminate in the external iliac nodes

"The lymphatics of the ductus deferens anastomose with those of the epididymis at its origin and with the lymphatics of the seminal vesicles, the bladder, and of the prostate at its termination. The author also notes that the lymphatics of the ductus deferens empty into the external iliac and hypogastric nodes

"Supraclavicular nodes. The normal collateral branches of the thoracic duct are the efferent collecting trunks from the intercostal nodes on the course of which the juxtavertebral nodes are found. These collateral branches, instead of terminating in the thoracic duct, all open into an independent prevertebral collecting trunk, this collecting trunk is then joined to both ends of the thoracic duct by its two extremities only, the trunk terminating above directly in the jugulosubclavicular junction or in a node of the transverse cervical chain"

The practical application of this is that if there is a metastatic left supraclavicular node there is probably a metastatic chain of nodes all along the course of the thoracic duct. This is not always the case as I have seen a left supraclavicular metastatic node disappear under irradiation and the patient remain well in spite of the fact that there was no irradiation of the thoracic duct

Because the lymphatics of the testicle generally drain into the abdomino-aortic nodes we most frequently find the first metastasis in the upper abdomen above the bifurcation of the aorta. This does not preclude the possibility of a lower abdominal metastasis as these are the glands (external iliac) which drain the

epididymis. The teratoma originating in the rete testis, at the junction of the testicle proper and the epididymis, may grow either toward the testicle or toward the epididymis, or involve both

The regional node involvement of the 37 cases, expressed in percentage, is as follows: inguinal, 4 cases, 10.8 per cent, pelvic or iliac, 14 cases, 37.9 per cent, lumbar, 20 cases, 54.16 per cent, celiac, 21 cases, 56.87 per cent, mesenteric, 7 cases, 18.95 per cent, mediastinal, 18 cases, 48.7 per cent, bronchial, 13 cases, 35.2 per cent, cervical, 13 cases, 35.2 per cent

A tumor of the testis rarely metastasizes to the inguinal nodes unless it has perforated the tunica vaginalis or capsule of the testicle. In Cases 4, 26, and 31 these nodes appeared after operation. This is significant as we believe that inguinal node involvement is almost always the result of cutting into the teratoma with the resultant implanting of tumor cells in the operative wound and a secondary involvement of the inguinal glands. In Case 16 the inguinal nodes were contralateral only. The explanation of this finding is not clear. However, this patient had generalized metastases

In 10 cases, or 27 per cent, there was node involvement which extended from the lumbosacral promontory to the left supraclavicular region

In 5 cases, or 13.5 per cent, in which the abdominal and mediastinal nodes were involved, the left supraclavicular nodes were not palpable

The mediastinal nodes were involved in 48.74 per cent of the cases. In the chest films observed there was no hint of mediastinal involvement in less than half of the cases

The bronchial and cervical nodes were each involved in 13 cases, or 35.2 per cent, but involvement in both regions occurred only 7 times, or in 18.95 per cent

In 7 cases in which the right testicle was the primary focus there were left sided supraclavicular so called signal nodes. In 6 cases in which the primary focus was in the left testicle there were left signal nodes

In many cases the center of the nodes or metastatic foci, especially those in the liver,

<sup>1</sup>Anatomy of the Human Lymphatic System, 1938

were broken down and hemorrhagic. In 5 cases of this type the peritoneal cavity contained bloody fluid in amounts up to 3000 cubic centimeters. This observation has been made at the operating table and may be very puzzling.

*Gross metastasis to the head and neck.* In 3 cases there was intracranial disease which did not involve the brain (meninges). In 3 other cases the brain was involved, which gives 16.24 per cent with intracranial involvement. This region was examined in less than half of these cases. This figure therefore, would be materially increased if the actual number of cranial examinations was known.

In Case 17 the spinal cord was involved. This case has been reported by Kennedy and Stevenson.<sup>1</sup> The thyroid was involved by metastatic disease only once it being the only cervical structure involved other than lymphoid tissue.

*Gross metastasis in the thorax.* The lungs were involved in 29 cases 78.37 per cent. The pleura was involved in 14 cases, 37.9 per cent. In cases of pulmonary metastasis the mediastinal nodes were involved 16 times 55.17 per cent. The bronchial nodes were involved 13 times, 44.9 per cent, when the lungs were involved.

In 2 cases 5.4 per cent, there was bilateral hemothorax. In 2 cases, 5.4 per cent, there was unilateral hemothorax. In 1 case there was bilateral chyloous thorax. Obstruction of the thoracic duct does not always result in chyloous fluid accumulation because this may be conducted to the blood stream by accessory ducts.

In 2 cases there was a discrete metastatic focus within the chest wall. In 2 cases there was intravascular extension into the right auricle. This will be referred to later. In 2 cases the presence of pulmonary tuberculosis was noted.

In a surprising number of cases the diagnosis following first admission to a hospital is pulmonary tuberculosis because of the cachectic appearance, weight loss, night sweats, loss of appetite cough and eventually blood stained sputum. Most of these cases showed no evidence of tuberculosis at postmortem exami-

nation and the clinical picture could be readily explained by metastatic teratoma testis.

Gross metastases were found in the abdomen in the following locations: diaphragm, 4 cases, 10.8 per cent; liver 28 cases, 75.8 per cent; spleen, 4 cases, 10.8 per cent; pancreas, 3 cases, 8.2 per cent; kidneys, 6 cases, 14.3 per cent; adrenals, 4 cases, 10.8 per cent; retroperitoneal mass, 22 cases, 59.57 per cent; gastro-intestinal tract, 2 cases, 5.4 per cent; genito-urinary tract, excepting kidneys, 4 cases, 10.8 per cent.

Where there was pulmonary involvement—29 cases—the liver was involved in 22 cases, or 75.86 per cent. The liver was involved in only 6 cases, or 21.43 per cent of the cases without lung involvement.

*Liver involvement.* Metastasis to the liver in most cases, must be blood borne. Therefore, there is no relation between the liver metastasis and the site of the primary tumor. This is borne out by the record. In 28 cases in which tumors were found in the liver the right testicle was the primary focus in 13 and the left testicle in 15 cases. This factor is extremely significant and to us an unexpected finding.

The gastro-intestinal tract was involved once by multiple discrete lesions and once by extension from a retroperitoneal mass into the duodenum.

The genito-urinary tract was involved intrinsically in 9 cases, or 24.3 per cent. The kidney parenchyma was involved by metastasis 4 times and by extension from a retroperitoneal mass once. Twice the involvement was bilateral and thrice unilateral. Frequently the kidney is embedded in a retroperitoneal mass but its capsule is a pretty effective barrier in preserving the integrity of the kidney. The kidney was hydropic by pressure of the tumor either upon the ureter or upon the kidney pelvis, four times.

In one case metastatic teratoma testis which involved the kidney parenchyma grew into the renal vein whence it extended into the inferior vena cava and spread superiorly into the right auricle and inferiorly into the right common iliac vein. In this same case



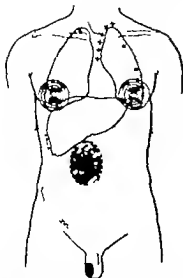


Fig. 1. Case R.R.W. Diagnosis: Primary embryonal adenocarcinoma with lymphoid stroma. Autopsy findings: Signal node disease, lungs riddled, pleura involved, mediastinal nodes, gynecomastia, liver metastasis, retroperitoneal mass extended from pelvic brim upwards.

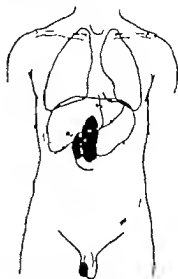


Fig. 2. Case K.H. Diagnosis: Primary embryonal adenocarcinoma. Postmortem examination revealed the following: Pulmonary disease, liver disease, retroperitoneal mass, invasion of duodenum, thrombosis of venous, mesenteric nodes.

CASE R. R. W. aged 33 years, was first seen at the Memorial Hospital, October 1933, with the following history: definite trauma to right testicle in 1922. Three years previously the right testicle became hard with no pain or swelling. Two months before he first noted nodes in the left side of the neck and gradual enlargement of the right testicle. He developed a productive cough with blood stained sputum. This was shortly followed by severe persistent backache. Seven weeks before he first noted bilateral painless enlargement of the breasts without secretion. He lost 30 pounds in weight in a period of 2 months.

The Aschheim-Zondek test revealed a high prolactin content. A positive Wassermann reaction was obtained in 1933 and treatment was instituted.

Postmortem examination was made on November 1933. Patient was a slightly emaciated white male with recent operative scar in the right groin. The right testicle had been removed. A bulky mass of tissue was present in the left neck. Both breasts were enlarged by palpable masses. The surface of the lungs was roughened as a result of studded areas of metastasis. The cut surface of the lungs showed marked congestion and the entire tissue of both lungs was riddled with metastatic areas from 0.5 to 3.0 centimeters in diameter. The liver was somewhat enlarged, congested, and contained two tumor areas. One of these was visible on the surface. Each measured about 0.5 centimeter in diameter both appeared hemorrhagic. The kidneys showed no abnormalities. The right testicle showed no abnormality. A disease as found at the site of the

left testicle which had been removed. Examination of the lymph nodes showed large tumor mass about 20 by 3 centimeters in retroperitoneal position extending from the pelvic brim along the vertebral column. The mass protruded more to the right than left side. The cut surface showed the same hemorrhagic areas as found in the lungs. Enlarged mediastinal nodes were found that contained tumor tissue, some measuring 3.0 centimeters in length. The mass of nodes in the left neck also contained the same type of tissue as the others. The brain showed no evidence of metastasis, except for a small nodule. Tumor was removed from each breast. It was tough, fibrous, and of a shaggy structure.

The anatomical diagnosis as teratoma of the right testicle with metastasis to the lymph nodes, lungs, liver and arachnoid.

The microscopical examination showed embryonal adenocarcinoma. The liver metastases showed change in structure more diffuse, some giant cells but there was no suggestion of chorionepithelioma. The breast showed gynecomastia. The opposite testis showed no Leydig cell hyperplasia.

CASE K. H. aged 34 years, was first seen at the Memorial Hospital July 1934, with the following history: Patient lost 60 pounds in the past year. Two months ago a gastro-intestinal series as reported as normal (Lenox Hill). One month ago patient first noted a mass in the right side of the abdomen. Three weeks ago laparotomy (Philadelphia) revealed an inoperable retroperitoneal, right tumor just beneath the duodenum. The post-

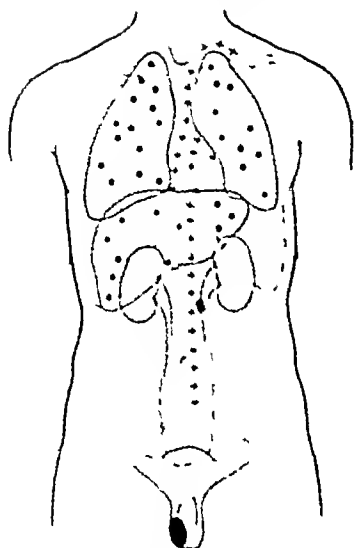


Fig. 3 Case 3 I H. Diagnosis: Primary diffuse embryonal carcinoma. Autopsy findings: Signal nodes in involved lungs riddled with miliary metastases; large tracheobronchial nodes eroded trachea causing subcutaneous emphysema; liver metastases; wall of left ureter chain of nodes from bifurcation of aorta to left supraclavicular

creas were not involved. No gynecomastia was noted. No Aschheim-Zondek test was made. The right testicle was small, hard and nodular—must have been the same at time of operation.

Postmortem examination was made September 18, 1924. The body was that of an emaciated young adult male. Slight jaundice was noted. There was a healed surgical scar 6 inches long, from navel to pubis. The abdomen was free from fluid and signs of inflammation. There was a firm tumor mass in the retroperitoneal region extending from the third lumbar vertebra up to the liver, adherent to the liver and the right kidney, and displacing the pancreas forward. A segment of the upper jejunum or duodenum was closely adherent to the tumor and ran along the upper surface. The tumor mass was 15 centimeters long by 10 centimeters wide by 7 centimeters deep. It was firm, yellowish, without evidence of necrosis in the center. It enclosed several large arteries and the vena cava. The duodenal segment was sectioned and there was disclosed a large ulcerating excavated area, 7 centimeters by 10 centimeters, where the tumor had invaded the wall and fungated into the lumen. The vena cava passed near the base of this excavated area and here there was complete thrombosis of the vein, the thrombus running up and for 4 inches, where it had been cut through. A few small separate metastases were present in the mesentery. The liver showed rather numerous small metastases up to 2 centimeters in diameter. The lungs showed several pea sized metastases. There was no pneumonia. The bronchial node was nega-

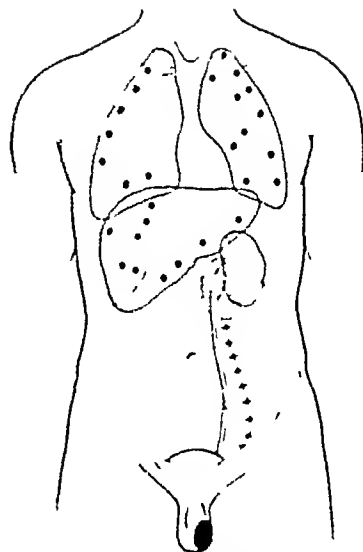


Fig. 4 Case 9 T C. Diagnosis: Primary diffuse embryonal carcinoma. Autopsy findings: Disease in lung and pleura; disease in liver; retroperitoneal nodes causing hydronephrosis.

tive. The right testis was about normal in size, but on section showed opaque tumor tissue invading about one half of the gland area and all the rete. The epididymis appeared to be involved by rather firm tumor tissue without enlargement. The tumor mass was yellowish and apparently much fibrosed. The left testis was normal.

The anatomical diagnosis was carcinoma of the testis, metastases to the retroperitoneal region, liver, and lungs, ulceration of tumor mass fungating into duodenum. There was thrombosis of the vena cava.

Microscopical examination of sections showed an embryonal adenocarcinoma becoming diffuse carcinoma in the primary and all secondary tumors. There was very marked necrosis of the tumor in all lesions. The cells were very large, polyhedral and elongated, with clear or vacuolated cytoplasm and very hyperchromatic nuclei.

CASE 3. L. H., aged 27 years, was first seen at the Memorial Hospital on December 5, 1931, with the following history. The right testicle was removed 12½ years previously for "blood tumor" which had been present for 3 months. He now complains of pain in the abdomen and back, nausea and vomiting, loss of weight and appetite. No gynecomastia present. The Aschheim-Zondek test was positive.

Postmortem examination, January 11, 1932, revealed no right testis. There was no sign of local tumor. Both lungs filled the chest cavity, were grayish, moderately emphysematous, and were riddled with miliary metastases throughout. These formed large confluent masses in the right lower lobe. The hilum nodes were greatly enlarged and were



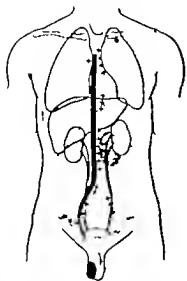


Fig. 5. Case a. C.G. Diagnosis: chondrosarcoma. Autopsy findings: Pulmonary foci, cns arypses obliterated, bronchial nodes, neoplasm in right atricle, neoplasm in inferior vena cava, retroperitoneal mass around left kidney spermatic vein obliterated, retroperitoneal disease extending to base of heart, hilaral nodes.

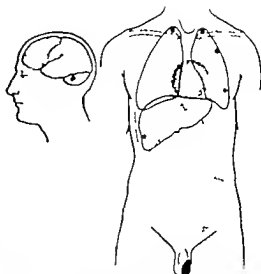


Fig. 6. Case 14. CS Diagnosis: Primary chori-epithelioma. Autopsy findings: brain metastases, pulmonary disease, anterior mediastinal disease, liver disease.

replaced by tumor which had secondarily invaded the trachea and primary bronchi at the bifurcation. This tumor was very soft, broken down, and may well have been the source of the interstitial emphysema. The node masses compressed the bronchi and vessels. The former yielded considerable thick mucopurulent material when sectioned. The stomach was pressed downward by an enlarged liver and metastatic deposits in the lesser omentum. The intestines, aside from downward displacement, were normal. The retroperitoneal nodes were completely replaced by tumor from the sacral promontory to the lung hilum and were continuous with those of the upper mediastinum. The kidneys were normal. The right ureter was normal. The left ureter showed an area of tumor metastasis which involved both the serosa covering and the lumen. The left testis grossly was normal.

The anatomical diagnosis was embryonal carcinoma of the testis, generalized carcinomatosis in vasion of the trachea and bronchi by metastatic node deposits with interstitial emphysema.

Microscopical examination showed diffuse embryonal carcinoma. Section of the thyroid showed cystic dilatation and colloid retention, of the testis marked diffuse hyperplasia of the cells of Leydig

CASE 9. T. C., aged 46 years, was first seen at the Memorial Hospital on December 6, '93 with the following history. He first noticed mass in the left testicle and left kidney region on September 5, '92. He had had back pain in the left upper quadrant for about year previously. The testicle had been

swollen and showed moderate jaundice. The abdominal lymph glands, described on the left retroperitoneal side up to the kidney, were hard, nodular, and hemorrhagic. On the right there was no enlargement. The lower pelvis, about the prostate and bladder was fibrosed and densely adherent to the posterior lateral walls. The left testis was absent, the right atrophic.

The anatomical diagnosis was metastatic embryonal carcinoma involving the abdominal lymph nodes, liver, and lungs, hydronephrosis, cholelithiasis, atrophy of the testis, right, and absence of left, jaundice.

Microscopical examination showed diffuse embryonal carcinoma with necrosis and hemorrhage, adenocarcinoma, atrophy of opposite testis with interstitial cell hyperplasia.

CASE 10. C. G., aged 37 years, was first seen at Bellevue Hospital, on February 5, 1919, with the following history. In October, 1918, patient had sudden pain in the right iliac region. The local medical doctor prescribed a cathartic and the pain disappeared but patient felt as if there was something obstructing the bowel in that region. He did not vomit. Soon after he started having cough, night sweats, evening rise of temperature, fatigue, loss of weight—30 pounds in 3 months. He gave no history of trauma, no history of gynecomastia. No Aschheim-Zondek test was made. The epididymis was enlarged and tender on the right.

Postmortem examination was made April 7, 1919, and showed the following. The chest was opened and two egg sized firm globular masses came into view in the region of the upper precordial area. The right side of the heart was opened and a large quantity of firm, raspberry colored clot escaped. Both lungs were large and heavy. Nodules were present and measured from 1 to 6 centimeters in diameter. These projected above the cut surface. They were friable, finely granular, contained innumerable and irregular outlined reddish specks which corresponded to hemorrhage. Others were reduced to soft, pulsatous masses. The peribronchial nodes were extensively infiltrated and the aorta was embedded in similar tissue. Practically the whole lower lobe of the right side was replaced by neoplasm. The left kidney was embedded in nodular tissue material. No intrinsic neoplasm was found on gross examination in either kidney or suprarenal gland. The right testicle tunica vaginalis contained considerable thin, straw colored fluid. The testicle was increased to the size of a hen's egg. On section, the upper extremity presented an irregularly outlined, firm, whitish, almost pearly, elevated tumor, scattered through the substance of which were moderate numbers of reddish specks. Just below this the testicle presented a large pulsatous, partly granular infiltrating growth which was dark cream colored. Lying to the side of this tumor, the epididymis was visible as a bean sized yellowish, finely angulated body. The spermatic cord was markedly thickened and infiltrated by tumor tissue. On section, the spermatic

vein was found to be the size of the little finger and was filled with a grayish red, attached clot. The retroperitoneal tissues were involved from the left external iliac vein to the base of the heart. The vena azygos was enlarged and filled with tumor tissue. When the liver was removed it was found that the vena cava was almost completely occluded by reddish, raspberry clot. The intima was thickened and attached to it was a quantity of finely granular, reddish, tumorous material. The left femoral vein was thrombosed with tumor tissue. The inguinal nodes on the left side were enlarged and faintly cream colored. The liver contained no gross metastasis.

The anatomical diagnosis was chorionepithelioma of the right testicle, extensive infiltration of the corresponding spermatic cord, with neoplastic thrombosis of the spermatic vein, extension of tumor clot into the auricle of the heart, massive pulmonary metastases, bilateral, extensive neoplastic infiltration of the perirenal connective tissues and of the tissues surrounding the aorta from commencement to bifurcation, neoplastic infiltration of tissues around the left common iliac artery and vein.

Microscopical examination confirmed the diagnosis of chorionepithelioma.

CASE 14. C. S., aged 15 years, was first seen at the Memorial Hospital May 24, 1935, with the following history. For past 2 months had noticed weakness, past 3 weeks, shortness of breath, pain in right shoulder and right side of chest. On May 10, 1935, roentgenograms of the chest had been made elsewhere and showed a large mediastinal mass. No cough or weight loss noted. Both testes were atrophic, about one-fourth normal size. There was no history of mumps. In view of the bulky intrathoracic metastatic tumor in a young man and in view of the atrophic testes, the Aschheim-Zondek test was suggested. It was made and showed a high prolactin content. There was no history of trauma and no gynecomastia.

Autopsy was performed June 24, 1935, and showed the following. The tissues of the anterior mediastinum were edematous. Overlying the entire anterior pericardium, attached thereto and to the diaphragm and fusing inseparably with the portion of the right lung overlying the pericardium was a bulky, soft, brownish, cystic hemorrhagic mass of tumor. It was too low for a typical thymoma and failed to surround the great vessels at the base of the heart. The heart itself was negative. Throughout the lung parenchyma were numerous similar tumor nodules. None communicated by ulceration with the dissected bronchi. Some appeared on the pleural surfaces and one was adherent with the parietal pleura over the ninth and tenth ribs on the right in the axillary line. The right visceral pleura showed gelatinous edema. Both testes were firm but small. In the left testis was a small, firm, elastic, whitish nodule about 4 millimeters in diameter,

<sup>1</sup>Previously reported by Craver and Stewart. J. Am. M. Ass. 1936 106:180-184.

separate from that was a somewhat smaller grayish mucoid looking nodule. The former looked like fibroma. The brain, scalp, and calvarium were negative. The meninges showed slight yellowish edema with xanthochromic fluid. No gross hemorrhage was present. A small hemorrhagic cortical metastasis about 1 centimeter in diameter was noted in the right occipital lobe in the superior lateral portion. Hemorrhagic metastases 3 centimeters in diameter easily enucleable were noted in left cerebellar hemisphere and were surrounded by pronounced yellowish gelatinous edema. No gross

obstruction was noted in the fourth ventricle. The lateral ventricles showed decided dilatation. The source of a spinal hemorrhage must have been

located low down. The pituitary gland was normal on gross inspection.

The anatomical diagnosis was chorionoma of left testis, fibroma of left testis, testicular trophoblastic tumor, primary mediastinal teratoma, (?) embryonal carcinoma of lung, metastases to lung, liver, brain, cerebellar edema, congestion of liver, spleen, and kidneys.

The microscopical examination revealed teratoma testis, primary consists only of adult mucous glands and cholesteatomatous cyst. It is not ascertainable malignant local residue metastatic choriocarcinoma—in the mediastinum, liver, brain, testicular trophoblastic and extreme interstitial cell hyperplasia and hypertrophy.

# ARTHROGRAMS OF HIP JOINTS OF CHILDREN

Dr ERIK SEVERIN, Stockholm, Sweden

IN the investigations now being carried out at the orthopedic clinic in Stockholm on the many unsolved problems concerning congenital dislocation of the hip, the arthrographical study of such hip joints has proved extremely useful. Because of its cartilaginous nature, a great part of the hip joint of a child is outside the scope of roentgen-anatomical studies, unless a contrast medium is used.

The literature on hip joint arthrography is scarce. Some authors have contented themselves with determining the shape and size of the caput from the arthrogram, in cases of congenital dislocation of the hip, the breadth of the isthmus has been ascertained together with the presence of ligamentum teres, etc. In his book *Untersuchungen ueber die Aetiology und Pathogenese der angeborenen Huftverrenkung*, however, Faber has given a clear description of how the free border of the cartilaginous acetabulum can be identified. He also points out how this identification provides further means of distinguishing between a normal hip and those in different stages of caput displacement: if the joint is to be styled normal, the border of the cartilaginous acetabulum should reach down laterally to the horizontal line through the Y-shaped cartilages or in its immediate vicinity, if this border is displaced upward a subluxation has developed, and when the caput has come away completely from the acetabulum, a complete dislocation results.

No one, however, has paid much attention to the details in the medial part of the arthrogram. In the hope of confirming the correctness of earlier arthrogram findings and also to add to our knowledge of the details found in arthrograms of the hips of normal children, we have carried out an investigation which is here discussed.

The material used consisted of arthrograms made at the Clinic and also of specimens of

hip joints from stillborn children at full term.

A mixture consisting of cinnabar and celloidin—film being dissolved in acetone—was injected into the hip joints of the postmortem specimens. For the sake of simplicity, this mixture will be called "cinnoidin."

As cinnoidin flows sluggishly, the injection was carried out by means of a metal syringe. The threadworm of the pistonshaft was passed through the nut at the end of the syringe so that the piston could be screwed forward with some force. The joint was punctured from the front, and a few small stitches were placed around the point of the syringe with silk. During the process of injection, the distention of the joint capsule was checked by the fingertip, to ensure that it was complete but not excessive. By the careful moving of the joint, the cinnoidin was distributed within it. The preparation was placed in a diluted formalin solution for some weeks to prevent it from drying. When the cinnoidin had solidified, and this could be determined by pricking with a needle, the arthrographic cast was checked by roentgenogram and subsequently dissected for comparison with the roentgen pictures. The bright red color of the "fixed" arthrogram facilitated dissection.

Complete agreement cannot be expected between the cinnoidin-arthrograms and those arthrograms made with perabrodil in clinical patients. Compared with perabrodil, cinnoidin flows slowly, and a good deal of the soft parts had been removed during dissection of the postmortem material. This should be taken into consideration in passing judgment.

Comparison of the clinical arthrograms with the cinnoidin preparations and their roentgenograms reveals the following:

At the insertion of the synovial membrane on the femoral neck, the contrast medium is collected into a ribbon round the neck (Fig 1, A).

The orbicular zone, B, appears as a circular attenuation in the contrast material, medial to the neck ribbon. The synovial membrane

From the Carolina Institute of Orthopedic Clinic, Vanföreskaanstalten, Stockholm, Professor Henning Waldenström, Director.

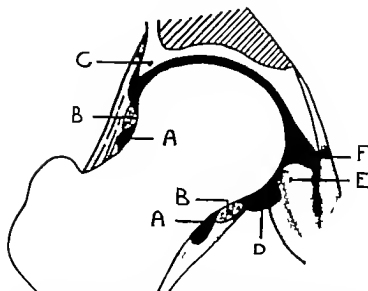


Fig. Arthrogram of hip joint (schematic drawing). *A*, fibrous band round the femoral neck, *B*, orbicular zone, *C*, fibrocartilaginous limbus, *D*, capsule pocket outside transverse ligament, *E*, depression of transverse ligament, *F*, recessus fossae acetabuli.

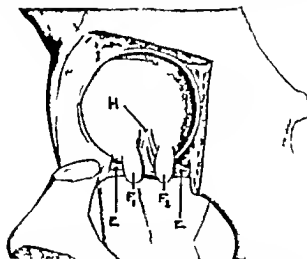


Fig. Arthrogram of hip joint seen from the medial side (schematic drawing: the bottom of the socket taken away). *E*, transverse ligament, *F*, recessus ventralis fossae acetabuli, *F*<sub>1</sub>, recessus dorsalis fossae acetabuli, *H*, ligamentum teres.

bulges out again above the orbicular zone and makes room for larger quantities of contrast material between itself and the caput, the shape and size of which is beautifully reproduced in the arthrogram.

In the upper parts of the joint, the fibrocartilaginous limbus, *C* protrudes into the contrast medium like a ploughshare. The recess situated outside the limbus is filled with contrast material up to the synovial mem-

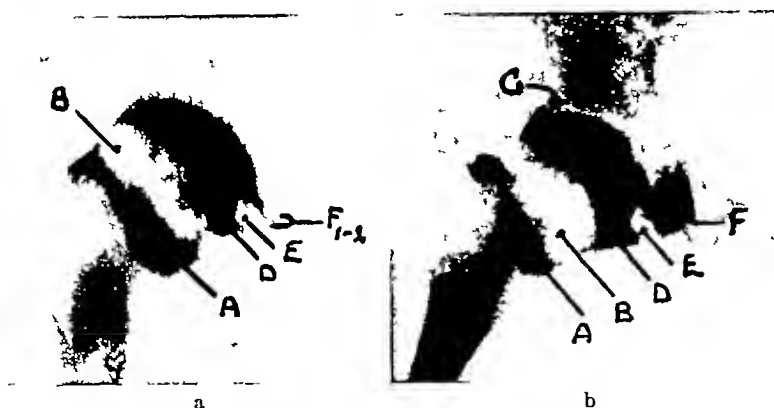


Fig 3 Arthrograms of the right hips of two stillborn children, taken with cannoidin. *A*, ribbon round the femoral neck, *B*, impression by zona orbicularis, *C*, impression by fibrocartilaginous limbus, *D*, capsule pocket outside transverse ligament, *E*, impression of transverse ligament, *F*, recessus fossae acetabuli (*F*<sub>1</sub>, ventral, *F*<sub>2</sub>, dorsal)

brane root some millimeters from the free limbus edge. The limbus thorn affords a sure base for the extent of the acetabulum upward. Beginning on the inside of the limbus, there is the space of the joint which *in vivo* normally has a thinner contrast material content than is to be obtained in the postmortem material.

Normally, then, the quantity of contrast medium between the femoral head and the acetabulum is very small, except medially. Here the contrast material is collected partly in the fossa acetabuli—i.e. medial, *F*, to the ligamentum transversum, *E*—partly in the relatively generous capsule pocket, *D*, which is to be found immediately outside the liga-

mentum transversum, *E*. The pointed fibrocartilaginous limbus merges into the ligamentum transversum at the incisura acetabuli.

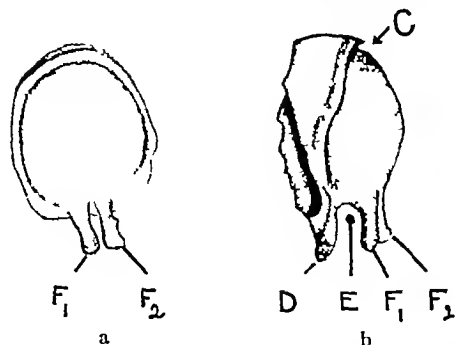


Fig 4 Preparation of the arthrogram seen in Figure 3b, seen from the medial, *a*, and ventral, *b*, sides. *C*, impression by fibrocartilaginous limbus, *D*, capsule pocket outside transverse ligament, *E*, impression of transverse ligament, *F*<sub>1</sub>, recessus ventralis fossae acetabuli, *F*<sub>2</sub>, recessus dorsalis fossae acetabuli.



Fig 5 Arthrogram of a child's normal hip joint. Perabrodil was used. *A*, Ribbon round the femoral neck, *B*, impression by orbicular zone, *C*, impression by fibrocartilaginous limbus, *D*, capsule of pocket outside the transverse ligament, *E*, impression of transverse ligament, *F*<sub>1-2</sub>, recessus ventralis et dorsalis fossae acetabuli.

Sectionally the ligamentum transversum is rounded and on account of its extension mainly in a dorsoventral direction seems, in pictures taken in a dorsoventral plane to appear in the contrast medium as a rounded impression (*impressio ligamenti transversi*) *E*.

According to Faber the quantity of contrast material in the bottom of the acetabulum is, normally extremely slight, but according to our investigations one should take into account the normal variations brought about by varying injection pressures, decreased muscle tonus under a narcotic, incongruity between the caput and acetabulum or the like. Naturally the quantity of contrast material contained in the fossa acetabuli also influences the size of the contrast medium pool in the bottom of the acetabulum.

The quantity of contrast medium which lies in the fossa acetabuli and which forces its way down medial to the ligamentum transversum, is parted at its lower tip into two prongs—a ventromedial, *F* and a dorsolateral, *F*<sub>2</sub>, the anatomical foundation of which are the two pouches, which the author names *recessus ventralis fossae acetabuli* and *recessus dorsalis fossae acetabuli*. The site of origin of the ligamentum teres, *H* from the medial side of the ligamentum transversum is joined to the bottom of the fossa acetabuli with a few firm tissues. If the contrast medium is subjected to pressure from above the soft parts in the fossa cannot recede uniformly but bulge into two pouches, whose divisional wall is supported by the aforementioned tissues between the bot-

tom of the incisura and site of origin of the ligamentum teres. Thus, both the resultant contrast prongs are usually projected onto one another but if they appear in the arthrogram it is possible, with their help, to point exactly to the spot where we should look for the origin of the ligamentum teres.

In cases of congenital dislocation of the hip, one or more of the arthrographic details noted may be distorted or obliterated through more or less extreme secondary changes.

#### SUMMARY

Casts, obtained by dissection after being photographed and compared with corresponding roentgen pictures, have helped to show where contrast medium is collected in arthrography of hip joints of normal children. The details of the arthrograms have been directly identified in the specimens. Comparisons have also been made with clinical arthrograms.

The extent of the cartilaginous acetabulum may be determined laterally with the aid of the limbus thorn, medially with the aid of the ligamentum transversum which at a suitable projection, appears in the contrast medium as a rounded impression (*impressio ligamenti transversi*). Time and again one sees the quantity of contrast medium situated medial to the ligamentum transversum, parted into two prongs by the origin of the ligamentum teres. These two prongs are enclosed in two pouches which the author names *recessus ventralis fossae acetabuli* and *recessus dorsalis fossae acetabuli*.

# THE IMPLANTATION OF SOLID PELLETS OF ESTROGENS IN THE TREATMENT OF MENOPAUSAL SYMPTOMS

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IT is the purpose of this paper to report the use of solid pellets of estrogenic materials in the treatment of 37 patients suffering from menopausal symptoms. Four patients with kraurosis and leucoplacia of the vulva have been similarly treated. In addition, pellets have been given to 4 patients with leucoplacia buccalis or chronic stomatitis, following out the work of Nathanson, who has treated successfully patients with leucoplacia by repeated injections of estrogens in oil. A single case of what appeared to be hyperfunction of the adrenal cortex was treated. In general, those suffering from menopausal symptoms have been greatly relieved by the pellets for periods varying from 5 months to more than a year. The patients with kraurosis have been somewhat improved but not cured. No effect has been noted on leucoplacia buccalis or chronic stomatitis. The only noticeable effects on the hirsute woman was the suppression of her scanty menstrual periods for 2 months.

In 1937 Deanesly and Parkes published their observations on the prolongation of estrogenic effects in capons by the implantation of solid crystals of estrone beneath the skin. Whereas 4 milligrams of estrone dissolved in sesame oil and injected subcutaneously into a brown leghorn capon caused the appearance of a narrow brown stripe on the growing black breast feathers of the bird, a smaller amount (3 mgm) implanted as a crystal beneath the skin resulted in a total change in color of the growing feathers to brown and this effect was continued for nearly 3 months. Similar prolongation of hormone effects was shown in castrated rats by the implantation of testosterone pellets.

The fundamental idea of using the almost insoluble steroid hormones in solid pellet form to obtain long continued hormonal effects has

been used subsequently by many investigators, with excellent results. Thorn's (11, 12) experiments using desoxy-corticosterone in cases of Addison's disease are well known. Howard and Vest and Hamilton have used pellets of testosterone propionate to good effect. More recently Hartman has reported a careful series of experiments on monkeys in which he used pellets of estrogens, progesterone, and testosterone. He records effects from a single 3 milligram pellet of theelin lasting for 4 months or longer.

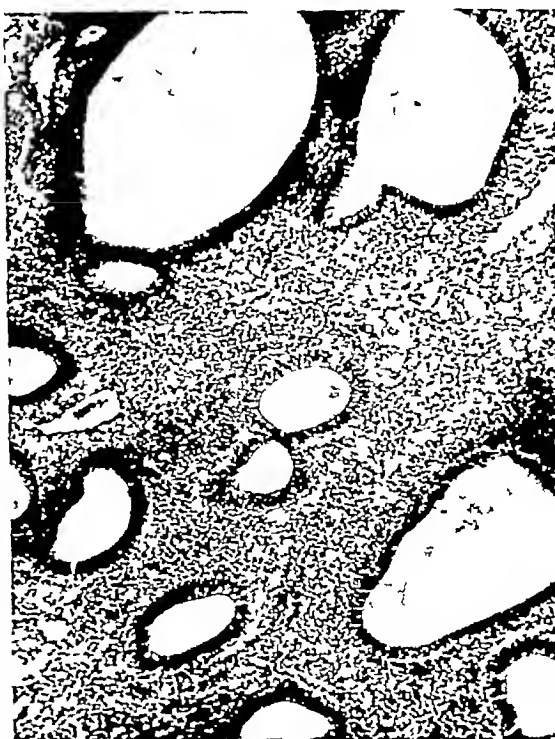


Fig 1 Endometrium from a woman treated with two 15 milligram pellets of  $\alpha$ -estradiol showing the typical Swiss-cheese type of endometrial hyperplasia produced by hyperestrogenism. The patient had had a spontaneous menopause 4 months before pellet implantation. Biopsy taken 7 months after therapy, 4 months after bleeding started.

From the Gynecological Services of the Memorial Hospital and the Roosevelt Hospital





Fig. 2 Vaginal smear from a girl of 10 who had been castrated, following x-ray therapy for dysgerminoma of the ovary. Note the predominance of deep cells and the absence of any large cornified epithelial cells with pyknotic nuclei.



Fig. 3 Completely cornified smear from the preceding patient one month after implantation of a 20 milligram pellet of estradiol.

Estrogens have been used in solid form to obtain very prolonged effects by Twombly who produced cancer in male mice of a susceptible strain (R III) with a single crystal of estrone given at 10 days of age and by Geschickter who produced mammary cancers in rats similarly treated. Bishop used a 14 milligram pellet of estrone in a patient suffering from menopausal symptoms and reported a reduction in the number of flushes from 10 to 12 a day to 4 to 6 a day, the effect lasting about 7 weeks. Salmon, Walter and Geist using crystals of  $\alpha$ -estradiol benzoate implanted 10 menopausal patients with 4 to 7 milligrams each and reported marked improvement in symptoms lasting from 60 to 98 days.

The experiments of Deanesly and Parkes seemed so striking that their application to women with menopausal symptoms immediately suggested itself and was begun on a

cautious scale in the fall of 1937 in our own clinic. Crystalline estrone was dissolved in ethyl alcohol and recrystallized, the crystals so obtained weighing from 1 to 24 milligrams. These were sterilized by boiling and introduced into the gluteal muscles by insertion through a small trocar. Later at the suggestion of Professor Parkes, pellets of estrone weighing 15 to 30 milligrams were used while all the recent cases have been treated with one or more 20 milligram pellets of  $\alpha$ -estradiol.<sup>1</sup>

These last pellets are firm and smooth, measure 3 by 2 millimeters, and are supplied sterile in glass ampuls. They are boiled for 3 to 5 minutes after removal from the tube as an extra check on their sterility and are inserted through a trocar size 10 French, such as is supplied by surgical supply houses for

<sup>1</sup>The crystalline estrone was obtained from the Schering Corporation through the kindness of Dr. Ervin Scheraga. The estrone pellets and the pellets of  $\alpha$ -estradiol were supplied by Dr. N. Machley of the A. V. Organics Company, London, and by Dr. R. D. Spenser of Radio-Organics, Inc., Natick, Mass. (J. T. these men are not indebted for their generosity.

tapping hydroceles The material has been inserted intramuscularly into the buttock through a novocain wheal, no incision or suturing being necessary The resultant scar is negligible

The first patients were treated with crystals of estrone alone Of these there were 4 There were 13 women who had crystals or pellets of pure estrone inserted first, followed at a later date with pellets of estradiol Fourteen patients had treatment either before or after pellet implantation with diethyl-stilbestrol given as tablets by mouth (1 to 2 mgm daily) or intramuscularly three times a week in doses of 0.2, 1.0, or 2.0 milligrams in oil A number of patients had previously had treatment with intramuscular injections of estrone in oil<sup>1</sup> before receiving pellets Finally there were 42 patients who received from 20 to 60 milligrams of  $\alpha$ -estradiol each, 23 of whom had no other form of estrogenic therapy

In treating patients suffering from menopausal symptoms, it has been impressed repeatedly upon us that one is dealing not only with the physiological lack of hormone but also with a complicated psychic pattern—the result of the patient's age, economic and social background, changing marital relationships, etc The latter symptoms are often curable simply by the frequent sympathetic questioning of the patient by the physician This is particularly true of the patients in the age group between 40 and 55 Some, in contrast, are very resistant to treatment of any kind, but in such cases we have found several times on questioning the patient carefully that clinical cure would entail the necessity of her going back to work or perhaps might result in a cut in home relief or in some way might be disadvantageous

Because it is so hard to get a reliable idea as to the degree of benefit from any form of therapy in these women, we have made it a rule to treat only patients with severe symptoms who were willing to count the number of flushes they had daily The effort required in this procedure eliminates many patients with mild symptoms and makes the results of therapy somewhat more objective Most of the patients have been followed from week to week

<sup>1</sup>Theclol-Parke Davis Company

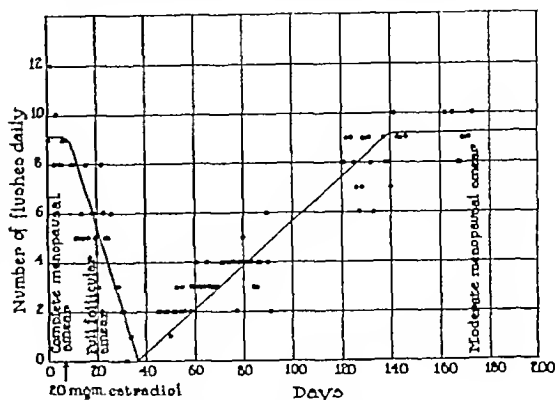


Fig 4 Record of hot flushes in the same patient showing complete disappearance in 1 month with a gradual return to the pretreatment frequency in 5 months

with studies of the vaginal smear In addition, the condition of the cervix and breasts, and other menopausal symptoms such as headache, dizzy spells, insomnia, crying spells, etc, have been noted at each visit

To illustrate the difficulty of accurately estimating the effect of medication, the first case may be cited, in which 4.8 milligrams of estrone completely abolished all hot flushes for at least 6 months though there was no change in the atrophic menopausal vaginal smear A number of patients have been cured of their symptoms merely by being required to count their flushes

In the other direction, a patient treated with 50 milligrams of estradiol and 100 milligrams of diethyl-stilbestrol, given both by mouth and intramuscularly, never showed any striking relief of symptoms but rather a slow improvement This effect seems significant when one knows that she is a confirmed attendant in the out-patient department of half a dozen other clinics A second patient showing no benefit complained, after 60 milligrams of estradiol in 4 months, that she felt so poorly that she ought to be on home relief but that the authorities would not agree that she was sick enough to stop working Her vaginal smear showed a full estrogenic effect

The most satisfactory results of treatment have been obtained among young people who are surgical or radiation castrates Three of these, 20, 25, and 30 years of age, have all shown complete cure for 3 to 6 months from

1 or 2 pellets of estradiol. In addition to their prompt reaction to treatment, they have failed to show the other psychoneurotic manifestations so frequently seen in the older patients.

Of the total of 46 patients treated, 17 were suffering from menopausal symptoms following surgical castration or hysterectomy. 14 had been treated with radium or roentgen rays while in 12 the symptoms followed a spontaneous menopause. Three patients were still menstruating. In general, the women who had been surgically castrated were more refractory to treatment than either of the other groups. They required from 1 to 3 pellets for complete relief of their symptoms, the average dose being 2; these usually being given within a month of each other. Those treated previously with radium were more easily relieved. They received only 1 pellet in 8 cases, 2 in 5 and 3 in 1; the average dose being  $1\frac{1}{4}$ . The 12 women who were suffering from postmenopausal symptoms after a spontaneous menopause were all treated with only 1 pellet, save in 3 cases, both suffering from kraurosis vulvae. The first of these was given two 20 milligram pellets a month apart, and the second 3 pellets. Of these 12 patients, 9 had uterine bleeding, starting 1 to 3 months after treatment, lasting from a few days to a year. This was severe enough in 1 case to require curettage and radium. Another should have been treated in the same way but refused. Three patients treated recently have had no bleeding. One of the surgical castrates bled 7 weeks after pellet insertion evidently from part of the lower portion of the uterus which had not been removed at the hysterectomy 2 months before treatment.

Women who have had a spontaneous menopause are relieved of their symptoms much more easily than surgical or radiation castrates, and this is what one would expect, since the ovary still has some activity even after the menstrual periods have ceased. However the uterine bleeding, which has occurred in three-quarters of these cases, would seem to contra-indicate treatment by pellets. In 5 of the patients who bled for a considerable length of time it was possible to obtain pieces of endometrium for study in 1 case by formal curettage under a general anesthetic, and in

the others by the use of a suction curette. All 4 patients showed the typical Swiss-cheese pattern of the endometrial glands typical of prolonged estrogenic stimulation. The microscopic section of one of these specimens is illustrated in Figure 1.

The pellet form of therapy has been very satisfactory in the patients treated with estradiol. All but one of the menopausal women have shown moderate to marked improvement or complete cessation of symptoms. This improvement has included abolition of hot flushes, improvement in sleep, great improvement in nervousness, cessation of crying spells, relief of headaches, and the advent of a feeling of well-being. The effect from a single implantation appears to last a variable length of time. Those patients in whom the effects seemed the most objective had relief for 5 to 6 months. In others relief lasted longer. It is our impression that the effect of estradiol in pellet form is more marked than anything we have been able to obtain with diethylstilbestrol or estrone in oil. Because of the expense of the latter drug for clinic patients, it may be that we have not administered it in large enough doses over long enough periods, but several patients, later treated satisfactorily with pellets, have had as much as 10,000 international units of estrone in oil 3 times a week for 3 weeks or longer. Diethylstilbestrol in our hands has given a high percentage of toxic effects. 6 of the 12 patients complained of nausea or abdominal pain when taking the drug by mouth. These symptoms have occurred occasionally even when the material was given by hypodermic injection.

In our hands the implantation of solid pellets of estrone have been practically without effect. One patient received four 15 milligram tablets at one time, another two 30 milligram tablets, another 65.4 milligrams as one 30 milligram pellet and about ten crystals, all without benefit.

As has been described by Papanicolaou and Shorr, the human vagina undergoes atrophy following the menopause with a marked thinning of the cornified layers of the epithelium. This thinning is accompanied by the appearance in the stained vaginal smear of leucocytes and large round cells with large nuclei, deep

cells" as they are called by these authors. These cells form the deeper or basal layers of the mucosa. In some cases the entire smear may consist almost entirely of them. In other cases, though the epithelial cells are large and polyhedral, the nuclei are quite large and palely staining. Under the influence of adequate amounts of ovarian hormone, the leucocytes tend to be greatly reduced in number or to disappear altogether, while the "deep cells" disappear completely. The epithelial cells become large and flat, and their nuclei shrink so that they are small, pycnotic, and deeply staining.

We have studied the vaginal smears in 35 of our cases and classified them as 0 to ++++, depending on the degree of cornification that they show. By 0 we mean a smear composed of small round cells with relatively large nuclei. Leucocytes may be present in abundance. Of the 26 cases in which smears were taken before therapy was begun, 11 showed this picture, one type of which is illustrated in Figure 2. When the smear contained only a few of these cells it was spoken of as +. Four pretreatment smears were thus classified. If the smear showed large polygonal epithelial cells with large pale nuclei and many leucocytes, it was labeled ++. There were 5 of these in the pretreatment smears. If there were few leucocytes and most of the epithelial cells showed pycnotic nuclei with less than half of them showing large nuclei, the smear was labeled +++. There were 6 of these. By ++++ we mean a smear consisting of large polygonal cells all of whose nuclei are small and heavily stained. Either no leucocytes or only a few are present (Fig. 3). This type of smear was not found in untreated cases.

In 24 of 30 patients treated with estradiol pellets in whom smears were taken after treatment, complete cornification was seen. Three patients showed smears classified as ++++. In 3 cases menopausal smears were found after treatment. The explanation for the failure of these patients to show a response in the vaginal smear is difficult. One patient certainly had a physiological response from the drug, for her breasts enlarged and the uterus increased in size. A second patient who had received 40 milligrams had complete relief

of hot flushes but continued to show deep cells in the smear. The third suffered from kraurosis. It has been our experience that patients with kraurosis require large doses to give any physiological response, and the fact that this woman failed to show any smear changes with one 20 milligram pellet corresponds with this clinical observation.

Several effects other than those it was desired to produce, in addition to the uterine bleeding already mentioned, deserve description. These include swelling and soreness of the breasts of mild to moderate degree lasting for a few days to a month. This occurred in about half of the patients. In 4 cases leucoplacia of the cervix was seen to develop following therapy. Biopsies in all of these cases showed only thickening of the epithelium without downgrowth into the underlying muscle. One patient who bled for almost a year after treatment developed a cervical polyp first, about 2 months after insertion of the estradiol. This was also true of the last case. Two patients complained of severe headaches for about a month at the time when it was judged that the effect of the pellet was wearing off. One patient with multiple fibromyomas of the uterus showed a definite increase in size of these tumors. The uterus before treatment was described as being about the size of a 2 months' gestation, whereas a month later it reached almost to the umbilicus. The same was true of a second patient though the growth was not quite so marked.

Finally, this report would not be complete without a word on the relationship of this form of therapy to cancer of the breast. As has been mentioned, cancer can be produced in male mice with single implantations of crystalline estrone. In the patients we are reporting, as much as 720,000 rat units of estradiol have been given to 1 patient. Because such an amount of drug might be thought dangerous, especial care has been taken to follow our cases, particularly with regard to the condition of the breasts and cervixes. In no case as yet has any mass developed in the breast. The only lesions of the cervix have been described. In this respect our experience agrees with that of Shorr and Papanicolaou (10) who report 452 patients treated from 1 to over 7

years with doses of 50,000 to 3,000,000 rat units of estrogenic material without a single case of cancer which could be attributed to the therapy they had received.

In our series there were 2 patients who had been treated with radium one 5 years and the other 7 years previously for carcinoma of the cervix. One girl of 20 had been treated for very extensive metastatic dysgerminoma of the ovary by x rays one year before estradiol therapy. None of these 3 patients has shown any evidence of reactivation of the tumor by the drug.

#### SUMMARY

1 Thirty seven menopausal patients, 4 cases of kraurosis vulvae 4 cases of leucoplacia buccalis and 1 case of adrenogenital hirsutism have been treated by the implantation of solid crystals or pellets of estrone or estradiol.

2 Estrone crystals and pellets have been ineffective in our hands.

3 Twenty-milligram pellets of estradiol have proved most efficacious for the prolonged alleviation of menopausal symptoms. The effective dose has been a total of 1 to 3 pellets given intramuscularly a month apart.

4 The full effect of the pellets becomes apparent in about 1 month. The effect lasts 5 months to a year as shown by subjective symptoms and vaginal smears.

5 Pellets are contra indicated in women with intact uteri, since they have caused bleeding (quite profuse and prolonged in some cases) in 9 of 12 such patients treated. No bleeding has occurred in patients who have received castrating doses of radium some time before estrogenic therapy.

6 Pellet therapy was only partially effective in 4 cases of kraurosis vulvae.

7 A woman with marked hirsutism had her menstrual periods inhibited for 2 months but

no improvement in the excessive hair growth was noted.

8. No case of carcinoma of the breast or cervix has been produced. Two cases of carcinoma of the cervix and one of dysgerminoma of the ovary have shown no reactivation of the disease by this form of medication.

#### BIBLIOGRAPHY

1. BISHOP, P. M. F. A clinical experience in oestrie therapy. *Brit. M. J.* 1938, 1: 939-941.
2. DRANKER, R., and PARKES, A. S. Factors influencing the effectiveness of administered hormones. *Proc. Roy. Soc. Lond.* 1937, Series B, No. 846, 2: 270-293.
3. GERSHBERG, C. F. Malignant carcinoma in rat with metastasis induced by estrogen. *Science*, 1939, 84: 39-47.
4. HAMILTON, J. B., and DORRMAN, R. L. Influence of the vehicle upon the length and strength of the action of the male hormone substance, testosterone propionate. *Endocrinology* 1939, 24: 712-719.
5. HARTMAN, C. G. Effect of testosterone on the monkey uterus and the administration of steroidal hormones in the form of Denstony-Parkes pellets. *Endocrinology* 1940, 26: 449-474.
6. HOWARD, J. E., and VERT, S. A. Clinical experience with male sex hormones. *N. Am. J. M. Sc.* 1939, 98: 821-826.
7. NATHANSON, I. T., and WEDDERBURN, D. S. The treatment of leucoplacia buccalis and related lesions with estrogenic hormone. *New England J. Med.* 1939, 321: 155-160.
8. PAPADOGIANNIS, G. N., and SMOKE, E. The action of ovarian follicular hormone in the monkey as indicated by vaginal smears. *Am. J. Obst. & Gynec.* 1936, 3: 806-831.
9. SALMON, U. J., WALTER, R. L., and CHITT, R. H. Prolonged therapeutic effect of subcutaneously implanted crystals of ovarian hormone in women. *Science*, 1939, 90: 162-163.
10. SMOKE, E., and PAPADOGIANNIS, G. N. Relation of estrogen to carcinogenesis in the human. *Acta Internat. Union against Cancer* (in press).
11. THORNTON, G. W., EMMETT, L. L., and EMBERTSON, H. Treatment of adrenal insufficiency by means of subcutaneous implants of pellets of deoxy-corticosterone acetate (a synthetic adrenal cortical hormone). *Bull. Johns Hopkins Hosp.*, 1939, 64: 15-166.
12. THORNTON, G. W. How to use M. P. EMBERTSON, K., and FURLO, W. M. *Bull. Johns Hopkins Hosp.* 1939, 64: 339-365.
13. TOWNSEND, G. H. Production of mammary carcinoma in male mice by single implantation of estrogen. *Proc. Soc. Exper. Biol. & Med.* 1939, 40: 430-431.

# CARCINOMA OF THE LOWER INTESTINAL TRACT

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IN the interval between January, 1922, and June, 1939, there have been 254 cases of carcinoma of the large bowel (including 2 of the appendix and 10 of the anus) in the University Hospital<sup>1</sup>. It was felt that a systematic study of the material presented by these cases would be of considerable clinical and pathological interest and would be representative of an average general hospital. Such a study is here presented with a satisfactory follow-up of approximately 97 per cent of the cases. We are greatly indebted to many busy practitioners and to the departments of vital statistics of the Baltimore City and State of Maryland health departments for invaluable assistance in following these patients.

## APPENDIX

There are 2 cases of adenocarcinoma of the appendix. Both occurred in white females, ages 44 and 49, respectively. Both presented the clinical picture of acute appendicitis. At operation the appendix was described as being gangrenous with abscess formation. The diagnosis of adenocarcinoma was made by the pathologist. One patient died in 3 days of peritonitis, the other survived operation to die in 2 years of generalized metastases.

## COLON AND RECTUM

There are 242 cases of adenocarcinoma of the colon and rectum. For purposes of convenience they are divided into 3 groups: those occurring in the right colon, the left colon, and the rectosigmoid and rectum. Of the 40 cases of adenocarcinoma in the right colon, 24 involved the cecum, 9 the ascending colon, 7 the hepatic flexure. Of the 63 cases in the left colon, 9 involved the transverse colon, 5 the splenic flexure, 9 the descending colon, and 40 the sigmoid colon. The rectosigmoid and rectum were involved in 139 cases.

From the Department of Pathology, School of Medicine, University of Maryland.

<sup>1</sup>Several inoperable cases were not proved by biopsy but were included in the study because the gross description at operation and the subsequent course justified the diagnosis of carcinoma.

**Age.** The highest incidence is undoubtedly in the age group 50 to 70 years, but youth is by no means ruled out, for 3 cases occurred in the age group between 17 and 19, 6 between 20 and 29, 14 between 30 and 39, 39 between 40 and 49, 76 between 50 and 59, 77 between 60 and 69, 26 between 70 and 79, and 1 between 80 and 89.

**Race and sex.** Of the patients with adenocarcinoma of the right colon, 29 were males, 11 females, 37 were of the white race, 3 of the black. Of those in whom adenocarcinoma occurred in the left colon, 35 were males, 28 females, 58 were white, 4 black, 1 yellow. Of those with adenocarcinoma in the rectosigmoid and rectum, 89 were males, 50 females, 133 were white and 6 black.

TABLE I — CHIEF PRESENTING SYMPTOMS

Symptom	Right colon	Left colon	Rectosigmoid and rectum
Constipation and/or diarrhea	13	41	89
Blood and/or mucus in stool	7	20	79
Abdominal pain	29	25	16
Palpable mass	16	13	5
Obstruction	12	11	18
Loss of weight	0	3	4
Anemia	8	1	0
Gaseous distention	0	5	0
Small stools	0	1	4
Rectal discomfort	0	0	26
Hemorrhoids	0	0	12
Urgency	0	0	7
Incontinence	0	0	4

**Symptomatology.** The chief presenting symptoms are given in Table I.

It was questioned whether there might be any relation between the duration of symptoms and operability. The average duration of symptoms of the adenocarcinomas occurring in the right colon in the entire group of patients was 10 months, in the operable group 5.5 months, in the inoperable group 11.7 months. The average duration of those occurring in the left colon in the entire group was 9 months, in the operable group 7 months, in the inoperable 10.5 months. The average duration was 10 months for those occurring in the rectosigmoid and rectum in the entire group.

years with doses of 50,000 to 3,000,000 rat units of estrogenic material without a single case of cancer which could be attributed to the therapy they had received.

In our series there were 2 patients who had been treated with radium one 5 years and the other 7 years previously for carcinoma of the cervix. One girl of 20 had been treated for very extensive metastatic dysgerminoma of the ovary by x rays one year before estradiol therapy. None of these 3 patients has shown any evidence of reactivation of the tumor by the drug.

#### SUMMARY

1. Thirty-seven menopausal patients, 4 cases of kraurosis vulvae, 4 cases of leucoplakia buccalis, and 1 case of adrenogenital hirsutism have been treated by the implantation of solid crystals or pellets of estrone or estradiol.

2. Estrone crystals and pellets have been ineffective in our hands.

3. Twenty milligram pellets of estradiol have proved most efficacious for the prolonged alleviation of menopausal symptoms. The effective dose has been a total of 1 to 3 pellets given intramuscularly a month apart.

4. The full effect of the pellets becomes apparent in about 1 month. The effect lasts 5 months to a year as shown by subjective symptoms and vaginal smears.

5. Pellets are contra-indicated in women with intact uteri since they have caused bleeding (quite profuse and prolonged in some cases) in 9 of 12 such patients treated. No bleeding has occurred in patients who have received castrating doses of radium some time before estrogenic therapy.

6. Pellet therapy was only partially effective in 4 cases of kraurosis vulvae.

7. A woman with marked hirsutism had her menstrual periods inhibited for 2 months but

no improvement in the excessive hair growth was noted.

8. No case of carcinoma of the breast or cervix has been produced. Two cases of carcinoma of the cervix and one of dysgerminoma of the ovary have shown no reactivation of the disease by this form of medication.

#### BIBLIOGRAPHY

1. BARNOR, P. M. F. A clinical experience in oestrogen therapy. *Brit. M. J.* 1934, 939-94.
2. DRAMNICK, R., and PARKER, A. S. Factors influencing the effectiveness of administered hormones. *Proc. Roy. Soc. Lond.* 1937, Series B, No. 834, 11, 179-198.
3. GERSCHWITZ, C. F. Mammary carcinoma in rat with metastasis induced by oestrogen. *Science*, 1939, 64, 35-37.
4. HAMILTON, J. B., and DUFFMAN, R. I. Influence of the vehicle upon the length and strength of the action of the male hormone substance, testosterone propionate. *Endocrinology* 1930, 24, 711-714.
5. HARTMAN, C. G. Effect of testosterone on the monkey uterus and the administration of steroidal hormones in the form of Deane-Parkes pellets. *Endocrinology* 1940, 26, 440-471.
6. HOWARD, J. E., and VERT, S. A. Clinical experiments with male sex hormones. *N. Y. J. M. Sc.* 1930, 198, 8, 1-86.
7. NATHANSON, I. T., and WENGBERGER, D. B. The treatment of leucoplakia buccalis and related lesions with estrogenic hormone. *New England J. Med.*, 1938, 31, 556-560.
8. PAPAGEORGIOU, G. N., and SIMON, E. The action of ovarian follicular hormone in the menopause as mediated by vaginal smears. *Am. J. Obst. & Gynec.* 1936, 3, 806-811.
9. SALAMON, U. J., WALLER, R. I., and GIBBY, S. H. Prolonged therapeutic effect of subcutaneously implanted crystals of ovarian hormone in women. *Science*, 1939, 90, 51-53.
10. SIMON, E., and PAPAGEORGIOU, G. N. Relation of estrogens to carcinogenesis in the human. *Acta Internat. Union against Cancer* (in press).
11. THORNTON, G. W., EMMETT, L. L., and ESTERSON, H. Treatment of adrenal insufficiency by means of subcutaneous implants of pellets of deoxycorticosterone acetate (synthetic adrenal cortical hormone). *Bull. Johns Hopkins Hosp.* 1930, 64, 51-106.
12. THORNTON, G. W., HOWARD, K. P., ESTERSON, H., and FROST, W. M. *Bull. Johns Hopkins Hosp.* 1936, 64, 339-364.
13. TOWNLEY, G. H. Production of mammary carcinoma in male mice with single implantation of estrone. *Proc. Soc. Exper. Biol. & Med.*, 1939, 40, 450-43.

20 per cent, systemic disease in 6, or 20 per cent

Of 18 patients dying of peritonitis 7 came to autopsy. Four of these had leakage at the operative site, 3 were apparently due to contamination at operation.

It was questioned whether peritoneal drainage played any part in the prevention of peritonitis. In 37 of the 79 cases resected peritoneal drainage was employed. Eight of these patients died of peritonitis. Only 2 of these 8 came to autopsy, 1 was due to leakage and the other was not. We doubt that there is any significance in these figures.

TABLE III —MORTALITY BY ERA OF THE 17 YEAR PERIOD

Year	Resected	Deaths	Percentage
1922-1929	20	6	30
1930-1935	23	10	43
1936-1939	36	14	39

TABLE IV —MORTALITY BY OPERATIVE PROCEDURE

Operation	Number cases	Deaths	Per cent
One stage abdominoperineal resection	20	10	50
Two stage abdominoperineal resection	0	5	56
One stage resection with end to end anastomosis or ileocolostomy	30	11	37
Two stage resection (preliminary cecectomy) with end to end anastomosis	4	1	25
Mikulicz resection	4	2	50
Posterior resection, rectum	12	1	8

*Prognosis of resected cases* Of the 79 cases resected 49 patients survived the operation. All of the 49 have been followed satisfactorily to December, 1939, except 1, and that one was followed for 5 years and has been considered as a 5 year cure. The end-results are presented in Table V.

Thus 24 patients have survived 3 or more years, of these 3 have died of recurrence and 1 of cerebral hemorrhage. One patient has recurrence after a lapse of 15 years. We feel that this could be justifiably considered another tumor. Of the 25 remaining cases, 11 have died of carcinoma in less than 3 years, 2 have died of heart disease, and 1 of cerebral hemorrhage within the same period of time. Eleven patients are still living and well, having survived varying periods of less than 3 years, 2 of these with known liver metastases.

TABLE V —SURVIVAL, OPERATION AND GRADE OF TUMOR

Survival— years	Operation	Grade <sup>1</sup>	Present status
16	One stage abdominoperineal	4B	Living and well
15	Two stage abdominoperineal	2B	Recurrence after 15 years
14	One stage resection, cecum	1A	Living and well
13	Posterior resection	3A	Living and well
11½	One stage abdominoperineal	2A	Living and well
11	One stage transverse colon	3B	Living and well
10	One stage cecum	2B	Living and well
10	One stage sigmoid	3B	Living and well
7½	Posterior resection	2	Living and well
7	Mikulicz descending colon	2B	Colloid. Died of recurrence
6	One stage abdominoperineal	2B	Living and well
6	Two stage abdominoperineal	3B	Living and well
5½	One stage sigmoid	2B	Living and well
5	One stage cecum	3B	Followed only 5 years
5	One stage cecum	2B	Living and well
4½	One stage sigmoid	2B	Living and well
4	Mikulicz transverse colon	2B	Living and well
4	Posterior resection	3B	Died of recurrence
4	Posterior resection	?	Died of recurrence
4	One stage abdominoperineal	2	Living and well
3½	One stage abdominoperineal	2A	Living and well
3½	One stage abdominoperineal	3C	Living and well
3	One stage abdominoperineal	1A	Living and well
3	One stage abdominoperineal	3	Died of cerebral hemorrhage

<sup>1</sup>Two methods of grading are employed. The one is the Broders method of grades I to IV, the other the Duke's method indicated by the letters A, B, and C. We apply the Duke's method as follows: A indicates the growth is limited to the mucosa and submucosa. B indicates involvement of muscularis, and C indicates peritoneal or regional node involvement.

*Survival by operative procedure* Of those subjected to posterior resection, 11 survived operation, 2 died of recurrence after 4 years and 6 after 3 years or less. Two patients survived a Mikulicz resection and 1 is living and well 4 years later, the other died of recurrence after 7 years. In the group of one and two stage procedures, 37 patients survived operation. Only 5 have died of recurrence in 3 years or less.

We feel that recurrence after resection indicates one of two things: (1) that metastases already present were overlooked at the time of operation. This is shown by 2 of the patients who died after operation in whom were found previously unrecognized liver metastases at autopsy. (2) That the excision of the growth at the operation was insufficient. This is apparent in the high incidence of recurrence in the posterior type of resections.

*Prognosis of inoperable cases* Of the 163 inoperable cases 47 patients died while in the



as well as in the operable group and in the inoperable group.

The individual variance is from 24 hours to 5 years. The figures given in the previous paragraph appear significant. The difference in chronology between the groups is probably related to anatomical position and physiology of each portion of the bowel. Only 4 cases were discovered incidentally. One cecum, during laparotomy for acute cholecystitis; another descending colon, at autopsy on a patient who died of obstruction following hysterectomy; a third, sigmoid, at autopsy on a patient who clinically had a psychosis and symptoms of a brain tumor; cerebral metastases and the fourth rectum following cystostomy for acute urinary obstruction. Nineteen cases were diagnosed on admission of patients to hospital as having an acute abdomen. Of these 8 were due to perforation of the growth, 10 to the associated inflammatory reaction without perforation, and 1 was due to an acute cholecystitis.

Roentgenograms were made in 80 patients: 21 of the right colon of which 18 were reported as carcinoma, 2 inflammatory; 1 negative; 40 of the left colon; 34 of which were reported as carcinoma—case reported as carcinoma of the transverse colon but found at operation lesion in the descending colon—6 negative; 19 of the rectosigmoid and rectum, 18 reported as carcinoma, 1 negative. Of the total of 80 cases, 70 or 87.5 per cent were reported as carcinoma; 2 or 2.5 per cent as inflammatory; and 8 or 10 per cent were negative.

One case was reported as carcinoma by roentgen ray and confirmed by laparotomy (but not by biopsy) which later proved to be diverticulitis. It is not included. In the 2 cases reported as inflammatory and in 7 of the 8 cases reported as negative the symptoms alone were still considered sufficient justification for laparotomy. Only 1 case reported as negative was missed entirely. This was the patient with a psychosis who was suspected of a brain tumor and in whom was found at autopsy carcinoma of the sigmoid with cerebral metastases.

**Operability.** Of the 242 cases, 79, or 33 per cent of the entire series, were operable; 11 or 27.5 per cent, of the 40 cases occurring in the right colon; 25 or 40 per cent, of the 63 in the left colon; 43 or 31 per cent, of the 139 in the rectosigmoid and rectum.

An operability of 33 per cent is low. This is partially explained by the criteria used for estimation of operability on the basis of metastases. There were 56 cases in which there were no demonstrable metastases but the local extent of the growth was the criterion for inoperability. There were metastases in regional nodes in 65 patients; in regional nodes and liver in 29 patients; there were regional and intra-abdominal metastases in 10 patients and generalized metastases in 3 patients.

There were 4 operable cases with metastases present in the regional nodes and liver. Two of these were missed at operation and were found at autopsy. The other 2 were recognized and the primary growth (rectum) was resected for relief of symptoms. Both are living and well, one 2 years and the other 1 year following operation.

TABLE II—TYPES OF OPERATION EMPLOYED

	Cases
<b>Right colon</b>	
One stage resection; ileh ileocolostomy	9
One stage resection; ileh ileocolostomy and supplementary ileostomy	
One stage resection; ileh ileostomy	
<b>Left colon</b>	
One stage resection; ileh end to end anastomosis	16
T. stage resection (periliminary cecostomy); ileh end to end anastomosis	1
One stage resection; ileh end to end anastomosis and supplementary cecostomy	
Mikulicz resection	4
One stage abdominoperitoneal resection (sigmoid)	
<b>Rectosigmoid and rectum</b>	
One stage abdominoperitoneal resection	20
T. stage abdominoperitoneal resection	9
T. stage resection; ileh end to end anastomosis	
Posterior resection	12

**Operative mortality.** Of the 79 patients operated upon, there were 30 or 38 per cent, operative deaths; 5 or 45 per cent, of the 11 cases in the right colon; 10, 38 per cent, of the 25 in the left colon; 15 or 35 per cent, of the 43 in the rectosigmoid and rectum.

**Chief cause of death.** Peritonitis—6 had obstruction—was the cause of death in 18, or 60 per cent, of the cases; operative shock in 6 or

<sup>1</sup>The case reported as negative here recently has been reviewed by Dr. Walter L. Hilly of the Department of Pathology. In the lesion was described but was considered inconclusive and the final impression was reported as being negative.

# LOCALIO, HINTON CHOICE AND USE OF COTTON FOR SUTURES

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## REFERENCES

- 1 BRODERS, A C New York State J Med, 1932, 32 667
- 2 DUKES, C E J Path & Bacteriol, 1932, 35 323
- 3 HUEPER, W C Ann Surg, 1932, 95 321, Arch. f  
klin Chr, 1930, 159 200
- 4 RANKIN, F W, and BRODERS, A C Surg, Gynec &  
Obst, 1928, 46 660
- 5 RANKIN, F W, and GRAHAM, A S Cancer of the  
Colon and Rectum, its Diagnosis and Treatment  
Springfield, Ill, and Baltimore, Md Charles C  
Thomas, 1939
- 6 RANKIN, F W, and OLSON, P F Surg, Gynec &  
Obst, 1933, 56 366
- 7 STEWART, F W, and SPIES, J W Am J Path, 1929,  
26 109

at Table V will confirm this for the Broders method The Dukes method appears significant, but it must be borne in mind that few cases in this series with peritoneal or regional node involvement were considered to be operable

Proper preparation of the patient has often been neglected Carcinoma of the colon and rectum is seldom, if ever, an acute surgical emergency Obstruction may well be one and at the same time should be a strong contra-indication to resection

## THE CHOICE AND USE OF COTTON FOR SUTURE MATERIAL

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**R**ECENT publications by Meade and Ochsner (8, 9) have focused attention on the use of cotton as a suture material In 600 B C Sushruta (2), the father of Hindu surgery, recommended the use of cotton sutures, and from time to time during the ages cotton has undoubtedly been used The earliest modern reference to the use of cotton is that of Ginkorski in 1936, who satisfactorily employed chemically sterilized cotton in 100 experimental animals and in 23 humans

The literature of the past decade has contained many articles (1, 4, 7, 10, 12) advocating the use of nonabsorbable suture materials Several objections have been raised to the use of catgut Among the more important of these are difficulty of sterilization, allergic sensitivity, variable absorbability, deleterious effects of chemicals, production of serum, delayed fibroblastic activity, and delayed wound healing Other criticisms are increased incidence of wound infection, dehiscence, postoperative herma, and unreliability of the square knot tied with catgut Silk presents none of these objections However, it has come into disrepute with some surgeons because slowly healing sinuses occur if an infection develops

Meade and Ochsner attribute these to the presence of infected granulations in the silk itself These authors state that cotton shows less tendency for tissue ingrowth between its fibers, and hence is less likely to produce sinuses in the presence of infection Cotton, therefore, partially obviates the most serious objection to the use of nonabsorbable sutures

Meade and Ochsner further recommend cotton as an inexpensive, pliable, easily sterilized, suture material Due to its high coefficient of friction, cotton is not likely to slip after the first throw of a square knot Furthermore it can be tied with reliable square knots After it is implanted in a wound, catgut, silk, linen, and cotton decrease in tensile strength in the order mentioned Meade and Ochsner have graded suture materials with the following criteria in mind amount and persistence of leucocytic infiltration, amount of serum and fibrin, appearance time of fibroblasts, and the length of time necessary to produce final healing Wounds sutured with cotton produced the least reaction and healed sooner, and therefore cotton was graded first, silk, linen, and catgut were graded in the order mentioned

hospital from the effects of the lesion. One hundred and sixteen left the hospital, and 2 of these later had resections at other hospitals. One died of the operation and the other died in 18 months of recurrence. Six of the 116 have not been followed. Five patients are still living after 6 years, 1 year 4 months 4 months, and 3 months, respectively. Aside from 3 in interesting survivals of 14 years, 13 years, and 6 years with electrocoagulation and radium and 1 survival of 4½ years with radium alone, there are no other survivals over 3 years and the average is 15 months. These unusual cases are discussed under radium treatment.

**Effect of radium.** Thirty-six patients with inoperable lesions received radium. Three of these were not followed. Twenty-seven of these have died in less than 3 years. Six patients survived 3 years or more and their histories are briefly presented in Table VI.

TABLE VI.—RADIUM TREATMENT

Survival in years	Grade	Dose in rads	Other treatment	Present status
14		2,300	Electrocoagulation	Dead of carcinoma
13½		2,300	Electrocoagulation	Living and well
6		2,400	Electrocoagulation	Living and well
4½	N biopsy	6,300	None	Dead of carcinoma
	No biopsy	2,075	None	Dead of carcinoma
2	(biopsy)	975	None	Dead of carcinoma

\*This patient was a 45 year old white female who was considered inoperable. She received radium treatment, electrocoagulation, and had hysterectomy performed for obstruction. Tumor was grade 3 biopsy. Thirteen years later patient returned complaining of rectal pain and discharge of pus and blood having been previously well. After another resection was decided that the tumor was operable and it was resected by posterior operation. This tumor was grade 3 and it was again biopsy that showed recurrence of the original growth. The patient has survived 6 years to date following the operation and is quite well.

It is interesting that the 3 best survivals with radium are grade 3 tumors. As these patients also received electrocoagulation treatment of the local growth we hesitate to draw any conclusions. The survival of 1 patient with an inoperable growth for 13 years, when the growth was resected, in spite of electrocoagulation and radium, leads to interesting speculation about our criteria for inoperability.

Of the 37 patients who received radium treatment for carcinoma of the rectum there is a record of biopsy confirmation of the diagnosis in only 19. In all but 1 of these unconfirmed cases patients have died with unmistakable carcinoma. In 1 case the lesion later

proved to be an inflammatory one and patient has survived 14 years without evidence of carcinoma being present.

#### SQUAMOUS CELL CARCINOMA OF THE ANUS

There are 10 cases of squamous cell carcinoma of the anus in the series. Five were in males, 5 in females. Seven were black and 3 white. The average age was 56 years, varying from 32 to 75. The average duration of symptoms was 11 months. The presenting symptoms were local pain in 7 cases, constipation and/or diarrhea in 5 cases, blood in the stool in 3 cases, and an anal mass in 3 cases.

Three were resected by posterior operation. One is living and well 3½ years after operation. This patient also has an associated lymphogranuloma inguinale. One is living and well 1 year after operation. One died of heart failure 4 months after operation. In 5 cases the lesion was electrocoagulation excised. Two of these patients died at operation, one of pulmonary tuberculosis, the other of general debility and infection associated with a neglected extensive growth. The other 3 died of recurrence and metastases in 2 years, 4 months, and 3 months respectively. The latter 2 had inguinal metastases at the time of operation. One patient had an extensive local lesion extending into the buttocks. No operative procedure was carried out but he received a course of radium. He has survived 6 months to date. One patient had metastases to the femur with an extensive local lesion. He received no treatment and died of carcinoma in 3 months.

#### CONCLUSIONS

Carcinoma of the colon and rectum is a relatively slowly growing and late metastasizing tumor. There is usually present an associated inflammatory reaction which clinically cannot be distinguished from the growth. Fifty per cent of the regional node biopsies at laparotomy are inflammatory.

Operability should be higher. The chances of survival of the untreated cases are poor at best. The chances of survival of the patient who has an adequate excision of the growth and survives the operation are good.

Pathological grading of these tumors is of no significance in this series of cases. A glance

Simple wetting of Handcraft cottons caused a decrease of 2 to 6 per cent. Handcraft cottons boiled for 10 minutes and tested while wet increased 2 to 11 per cent, drying caused decreases of 2 to 23 per cent, rewetting or re-boiling for 10 minutes re-established the original increase provided the cottons were tested while wet. Boiling Handcraft for 20 and 30 minutes caused no significant change if tested wet, drying, however, decreased the tensile strength 2 to 23 per cent. This decrease could be abolished by rewetting for 10 minutes in all the sizes except No. 000 and No. 00, which continued to show decreases of 10 per cent and 12 per cent in spite of rewetting, after having been boiled for 30 minutes. Throughout these tests, these cottons varied 7 to 37 per cent. Monarch, Kerr, Clark, and American Thread and LeRoy mercerized cottons showed similar trends of increased tensile strength after boiling, if tested wet, decreased tensile strength below control figures if allowed to dry, and increases above control figures if rewet. The increases were more marked than those observed for Handcraft cottons.

Determination of actual diameters varied considerably for cottons of different manufacture, but of the same stated size.

#### ANALYSIS OF STUDY

From the data presented, it can be readily seen that cottons of the same number but different brands vary considerably in their actual diameters and tensile strengths. This variation is not always due to greater diameter, for certain brands of cotton of lesser diameter have a greater tensile strength.

The choice of cotton suitable for surgery is dependent on several factors, and the surgeon is cautioned against the use of just any cotton. The cotton chosen should have the greatest tensile strength for its actual diameter, manufacturers' sizes and grading being variable and unreliable.

In order that the surgeon utilize the greatest possible strength of cotton and thereby use the finest possible suture, we suggest that cotton be sterilized by boiling 10 to 20 minutes and used while wet. The method employed at the New York Post-Graduate Hospital, which has been found simple and convenient, con-

sists of winding cotton on machine bobbins which are boiled with the instruments. After sterilization, the bobbins either can be kept wet by immersion in sterile saline or, if allowed to dry, can be wet just prior to use. Individual ties are removed from the bobbin by the operator and individual sutures are removed by the nurse.

For ligature of small blood vessels, Handcraft No. 000 cotton (0.007 inch) with a tensile strength of 2.5 pounds has been used. Larger blood vessels are ligated with Handcraft No. 00 (0.0075 inch) or Handcraft No. 0 (0.0085 inch) with tensile strength of 2.75 and 3.25 pounds, respectively. Fascia and peritoneum have been sutured with either Handcraft No. A-40 (0.012 inch) with a tensile strength of 3.75 pounds or Kerr No. B-36 (0.0115 inch) of a comparable tensile strength. The same cotton has been employed for intestinal anastomosis. Heavier cottons have not been found necessary, provided interrupted sutures are used. The holding ability of any suture is limited by the tensile strength of the tissue (5, 11) and hence the tensile strength of any suture should not exceed that of the tissue in which it is placed. The tensile strength of a suture line of interrupted sutures, provided a sufficient number of sutures are used, may be made equal to that of the tissue, although the tensile strength of the materials used be less than that of the tissue (6).

All sutures and ligatures were tied with true square knots and cut 1 to 2 millimeters from the knot. No difficulty was encountered in the use of wet sutures and ligatures.

The very low cost of cotton makes it practical to discard all unused material. To avoid confusion and error it is suggested that cottons of different sizes be dyed different colors and iron dyes be used in preference to coal tar dyes.

The variation in tensile strength of cotton may possibly be corrected by the manufacture of better surgical cottons, however, if interrupted sutures are used, the disadvantage of this variation will diminish. Of the cottons tested, those which best meet the criteria enumerated are Gudebrod Brothers Handcraft Nos. 000, 00, 0, and A-40, and Kerr's larger sizes Nos. A-40, B-36, and C-30.

The present study was undertaken to determine the type and brand of cotton best suited to surgery and the most efficacious method of sterilization. Thirty-six grades of cotton of 8 different brands, 24 grades of silk of 3 brands, and 5 grades of linen of 1 brand were tested. Studies were done on a Suter angle strand tester. The tensile strength of 10 consecutive single strands was determined. The average and the percentage variations of these 10 readings were calculated. The sutures studied were tested as they came from the manufacturer also after autoclaving after wetting after boiling, and tested wet after boiling and tested dry after boiling drying and rewetting and after boiling drying and reboiling. The average tensile strength of the materials as they came from the manufacturer was accepted as a base line and the percentage change in tensile strength after exposure to the various conditions enumerated was calculated.

#### SILK

The variation in tensile strength for braided serum proofed silk was below 10 per cent, and for twisted silk below 20 per cent. The tensile strength of Deknatel serum proofed silk increased after autoclaving. After 40 minutes the increase was 3 to 10 per cent, after 80 minutes 6 to 12 per cent, and 5 to 18 per cent after 120 minutes. Paré serum proofed silk showed no change after 40 minutes of autoclaving, an increase of 0 to 13 per cent after 80 minutes, and changes of minus 3 per cent to plus 6 per cent after 120 minutes.

Paré serum proofed silk of the various sizes when boiled for 10 minutes and tested while wet, decreased in tensile strength 0 to 25 per cent. If the same material was allowed to dry it increased in tensile strength 0 to 25 per cent, rewetting decreased the tensile strength 0 to 25 per cent. Champion twisted untreated silk, when boiled for 10 minutes and tested wet, decreased in tensile strength 18 to 39 per cent; this decrease was reduced to 0 to 16 per cent after drying. Autoclaving or boiling did not change the percentage variation of any of the silks tested.

#### LINEN

Linen autoclaved for 40, 80, and 120 minutes decreased in tensile strength 0 to 18 per

cent. The increase in tensile strength of No. 50 linen is not significant. Linen boiled for 10 minutes and tested wet increased 8 to 34 per cent. This increase was practically abolished by drying and was again apparent after rewetting. The percentage change of dried previously boiled linen was plus 0 to 8 per cent, and for the same material after rewetting plus 16 to 30 per cent. The percentage variation in tensile strength of the linens studied was 10 to 51 per cent.

#### COTTON

Handcraft cottons decreased 4 to 23 per cent after autoclaving for 40 minutes, 9 to 23 per cent after 80 minutes, and 5 to 23 per cent after 120 minutes. The percentage variation of Handcraft cotton was 6 to 44 per cent. Serum proofed cotton of the same brand was 12 to 35 per cent weaker, but the smaller sizes, No. 000 and No. 00 increased 4 to 15 per cent after autoclaving and the larger sizes decreased 2 to 33 per cent.

Monarch cottons decreased in tensile strength 3 to 10 per cent after 40 minutes of autoclaving, 2 to 9 per cent after 80 minutes, and 0 to 11 per cent after 120 minutes. Monarch No. 0 increased 4 per cent and 7 per cent after 40 and 120 minutes of autoclaving, respectively. These cottons varied in tensile strength 3 to 38 per cent.

Kerr cottons decreased 4 to 10 per cent after 40 minutes of autoclaving and, except for No. 00 to 60 which decreased 7 per cent, showed no significant change after 80 and 120 minutes of autoclaving. These cottons varied 7 to 39 per cent.

Clark cottons showed changes of plus 3 to minus 11 per cent after 40 minutes of autoclaving, plus 3 to minus 20 per cent after 80 minutes and plus 4 to minus 11 per cent after 120 minutes and varied 6 to 40 per cent.

Climax cottons decreased 0 to 11 per cent after autoclaving and varied 11 to 24 per cent. American Thread Company mercerized decreased 0 to 11 per cent and varied 11 to 24 per cent. LeRoy mercerized increased 6 to 9 per cent after autoclaving for 40 minutes and except for a decrease of 9 per cent in the No. 000 size after autoclaving for 80 minutes showed no further significant change. LeRoy cottons varied 6 to 35 per cent.

Simple wetting of Handcraft cottons caused a decrease of 2 to 6 per cent. Handcraft cottons boiled for 10 minutes and tested while wet increased 2 to 11 per cent, drying caused decreases of 2 to 23 per cent, rewetting or re-boiling for 10 minutes re-established the original increase provided the cottons were tested while wet. Boiling Handcraft for 20 and 30 minutes caused no significant change if tested wet, drying, however, decreased the tensile strength 2 to 23 per cent. This decrease could be abolished by rewetting for 10 minutes in all the sizes except No. 000 and No. 00, which continued to show decreases of 10 per cent and 12 per cent in spite of rewetting, after having been boiled for 30 minutes. Throughout these tests, these cottons varied 7 to 37 per cent. Monarch, Kerr, Clark, and American Thread and LeRoy mercerized cottons showed similar trends of increased tensile strength after boiling, if tested wet, decreased tensile strength below control figures if allowed to dry, and increases above control figures if rewet. The increases were more marked than those observed for Handcraft cottons.

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In a comparison of the tensile strength of suture materials before sterilization, if the actual diameter in inches is used for comparison size for size, silk has the greatest tensile strength. The tensile strength of silk increases slightly after autoclaving but decreases after boiling if tested wet. When one considers the decrease in tensile strength of wet silk and the increase in strength of wet cotton which is what actually occurs, in a wound, size for size, silk and good cotton are comparable.

During the past 5 months more than 50 major surgical procedures have been performed with the use of cotton throughout. These include gastric resections, colon resections, radical mastectomies, cholecystectomies, appendectomies, thyroidectomies, hernioplasties, suture of a perforated duodenal ulcer and pelvic procedures.

In these cases, cotton was used in 8 in the presence of infection. Three developed wound complications, 2 of which were wound infections in cases of acute gangrenous appendicitis which healed without sinus formation and the third a draining sinus of 5 weeks' duration in a case of tuberculous lymphadenitis from which pieces of cotton were extruded. Wound healing in the remaining cases has been excellent.

The cost of cotton makes it possible to perform a major surgical procedure for a few cents as compared with twenty-five cents to a dollar and a half for silk, one to three dollars for catgut. In institutions with active surgical services the use of cotton can effect a saving of several thousands of dollars a year.

#### CONCLUSIONS

1. Cotton chosen for surgical use should be limited to that showing the greatest tensile strength for the smallest diameter and the least variation.

2. Cotton should be boiled 10 to 20 minutes and used while wet.

3. Cotton has been shown to decrease in tensile strength after autoclaving and to increase after boiling provided it is tested while wet. If allowed to dry after boiling, cotton decreases in tensile strength. This decrease can, however, be abolished by rewetting or reboiling.

4. The principles of silk surgery advocated by Halsted should be adhered to in using cotton.

5. Cotton has been used in more than 50 major surgical procedures and has been found to be a satisfactory and economical suture material.

#### BIBLIOGRAPHY

- BARCOCK, W. W. *Text. Catgut suture*. *Am. J. Surg.* 935, 27-67.
- BRIDGES, A. R., K. K. L. *The Sashira Sashira*. Calcutta, 1907.
- CRITCHFIELD, V. M. Cotton thread. *Verstalt. Kib.* 936, 44-47.
- HALSTED, W. S. The employment of fine silk in preference to catgut and the advantages of transcending tissues and vessels in controlling hemorrhage. *J. Am. M. Ass.* 913, 60-9.
- HARVEY, S. C., and HOWES, E. L. The strength of the healing wound in relation to the holding strength of the catgut suture. *New England J. Med.* 936, 300-305.
- HOWES, E. L. The immediate strength of the sutured wound. *Surgery* 940, 7-24.
- KRAHSEL, CORNELIUS. Suture material. review of recent literature. *Internat. Abstr. Surg.* 936, 67-74.
- MEADE, W. H., and OCHSNER, ALTON. Spinal column as suture material. *J. Am. M. Ass.* 936, 30-36.
- Idem. The relative value of catgut, silk, linen, and cotton as suture materials. *Surgery* 940, 7-45.
- MILBURN, F. L. Infection in clean operative wounds; nine year study. *Surg. Gynec. & Obst.* 915, 801-804.
- SHARON, PHILIP. The silk technique. *Surgery* 940, 7-9.
- WHEELER, L. O. The choice and use of ligatures and suture material in the repair of clean surgical wounds. *Internat. Abstr. Surg.* 936, 69-109.

# THE PREVENTION OF HUMAN BITE INFECTIONS

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THE devastating effects of infection by organisms from the mouth of the human, especially when it involves the hand, is commonly termed "human bite infections" even though the original trauma is not inflicted by the teeth. The gangrenous sloughing infection of the hand so well described in the classic work of Mason and Koch is not so common as one might suspect from the frequent contamination of wounds by mouth organisms. The incidence of contamination of wounds by mouth organisms is undoubtedly great due to the frequency of thumb sucking, hangnail biting, and other habits which bring saliva into contact with wounds. Since the incidence of infection from such contamination is low, it is quite usual that the patient, and sometimes the doctor as well, underestimates the importance of such infections when they occur. Once infection has resulted from such contaminated wounds, the treatment is so difficult and so likely to result in loss of tissue and function that prophylaxis is important. Efforts to prevent infection have generally been quite radical. Bates reported the use of electrocauterization in 100 cases of early human bites with extension in but 1 case. Lowry reported 122 cases treated early by cauterization or by excision. Of these 93 involved the fingers or hand, but 55 of the 122 cases were observed until complete healing resulted, the average time for healing being 14 days. Cauterization by heat or chemicals is advocated by Dimtza, Dunn, Welch, McMasters, and others, as preferred preliminary treatment. In 1930, Mason and Koch suggested that immediately after a human bite injury, the wound be cleansed gently but thoroughly with soap and water and then débrided only of obviously damaged tissue be performed. This simple procedure which does not add material-

ly to the devitalization of tissue appealed to us as of fundamental importance. Accordingly, we have applied this treatment to the patients we have seen at the Detroit Receiving Hospital during the past 2 years. The routine procedure adopted was as follows. The area about the wound was carefully washed with soap and water after which the wound was gently but thoroughly sponged with soap and water for 10 minutes. When the injury was on the hand an effort was made to determine the extent of the injury, but the wound was not probed. Function of the fingers was noted and if injury to a tendon or joint space was evident the tissue was retracted gently and irrigated with physiological salt solution. If injury was evident in the extensor tendon or joint space, the wrist was splinted in hyperextension. Such wounds were dressed in dry sterile gauze and no attempt made to repair the tendon or joint capsule. When there were associated fractures these were splinted, and, in addition, in the case of compound fractures of the phalanges, the wounds were washed and then irrigated with physiological salt solution and saline compresses applied. No effort was made to close the wounds other than to hold the tissues loosely in approximation by means of the dressing. Patients with compound fractures in association with human bites were hospitalized for observation.

Human bites occurring in other parts of the body, especially the nose, ear, and lip were carefully cleansed with soap and water, devitalized tissue carefully débrided and the wound sutured, if this were possible, without too much tension.

While this was the routine followed in the majority of cases, slight variations from this technique were occasionally made, chiefly because early after the routine was instituted it was difficult to change technique and viewpoint immediately. Reliance on antiseptics frequently inaugurates a ritual which is changed slowly and with difficulty.

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TABLE I.—TYPE OF PRELIMINARY TREATMENT  
AND RESULTS  
(Statistics for year)

Fracture					5	Total
	a	b	c	d	e	
Finger	1					1
Wrist com- pound fracture						
Knuckle		14				14
Palm						
Forearm						
Arm						
Shoulder						
Forehead						
Chin	6					6
Lip						
Nose						
Ear			1			1
Repet						
Abdomen						
Back						
Thigh						
Total	31	20	14		1	66

**Comments**

1. Treated by soap and water cleansing.
2. Treated by soap and water cleansing with primary suture.
3. Treated by soap and water followed by phenol and alcohol.
4. Treated by phenol or nitric acid without washing.
5. Cases refused treatment.
- a. Reamended clean.
- b. Evidence of suppuration but did not suppurate.
- c. Becoming grossly infected.
- d. Did not return for follow-up.

One hundred and fourteen cases of human bites were seen within a few hours after injury. 81 of which were treated strictly by the procedure here outlined, the remaining 33 having some variation of the procedure. Table I gives detailed information concerning these cases.

In none of the 81 patients treated by the method outlined were there any whose wounds became infected, except 3 over the knuckle which were sutured. Seven of the 14 patients who were treated with phenol and alcohol developed more evidence of inflammation than usual wounds became red, swollen and indurated but did not suppurate. Two patients with knuckle injuries, which were cleansed and sutured, required hospitalization. One returned 8 hours after the preliminary treatment. The

sutures were removed and wet dressings applied. Twelve hours later drainage was advised but the patient left the hospital against advice. The second patient came back 4 days after preliminary treatment and required drainage of a seropurulent exudate from the dorsal subaponeurotic space and excision of a portion of the extensor tendon. The hand was splinted in hyperextension and saline soaks were applied. The wound healed well and resulted in a normally functioning hand. One other hand was sutured but the patient did not return therefore the results are unknown. Nine other patients were admitted to the hospital for observation immediately after preliminary treatment.

The results in this group of cases have been gratifying especially in comparison to former experiences with cauterization, excision, or extensive cleansing with strong chemical agents. The comparison of these results with those in the literature in which radical prophylactic measures have been taken, have confirmed our belief that observation following cleansing of the wound with soap and water within the first few hours after the injury is the method of choice for prophylaxis of human bite infections. We are impressed also that by this means the healing time of the wound is shortened and tissue destruction minimized. In 35 patients the average time for complete healing was 7.8 days. In 60 other patients it was felt that healing had progressed sufficiently far to discharge them in an average time of 4.9 days.

The recognition of human bites on the body is generally easy for there are usually abrasions, contusions, petechiae, and tooth marks present. Those on the nose, finger or knuckle may be more difficult to recognize. Over the knuckle there is usually a clean penetrating wound  $\frac{1}{2}$  to 1 centimeter long, which may appear to be superficial but if the patient will make a fist it frequently will bring a partially severed tendon into view or reveal an opening into the joint space. It is important to know the extent of the injury but not to the point where probing is indicated. This may not only fail to disclose small openings in the underlying tissue but it may result in the accidental spread of infection to a deeper layer

or open the joint space. It seems better to wash the wound and treat it kindly and gently. Daily observation of the injury to note inception of infection is indicated. In this group of cases there was one patient with an extensor tendon completely divided, as ascertained by the function of the fingers. No attempt was made to suture the tendon or close the wound, as we believe that this is contra-indicated in such potentially infected wounds. It is a good rule to consider any small penetrating wound on the hand as a human bite until proved otherwise, especially if this seems likely from the appearance of the wound, for it is a mistake to close such wounds primarily.

Bites on the fingers are generally on the distal phalanx. They vary from simple abrasions to compound fractures. In our series there were 3 of the latter. It is of interest that in each case the teeth penetrated the nail and did not leave any mark on the palmar surface. Bites on the distal phalanx are potentially dangerous and should be watched for the development of a felon or tendon sheath invasion. One case was seen in which the flexor tendon sheath had been opened and the tendon partially severed, but infection did not occur.

Injuries to the lip ranged from penetrating wounds to almost complete avulsion, the latter being more common. Many of these wounds result from the patient's own teeth during fighting, others, which were usually more extensive, resulted from bites by others. The amount of tissue removed varied considerably but in most instances removal extended into 1 or 3 centimeters. In 1 case an immediate pedicle graft was done and a good result obtained. In the other patients, in whose cases smaller amounts of tissue were missing, the wounds healed nicely by granulation without notable deformity.

For the most part, bites of the nose were extensive, going through the ala, severing the cartilage, the severed portion being attached only loosely over the bridge of the nose. Before a more careful study was instigated, no effort was made to get a cosmetic result

because the danger of infection with extension via the infra-orbital vessels was feared. Since we have utilized careful cleansing, we have felt that loose approximation is permissible and have seen no ill results to date. Bacteriological studies and smears were not made in this group of early cases, and we have no data regarding the degree or type of contamination present.

#### SUMMARY

One hundred and fourteen cases of human bite given prophylactic treatment within the first few hours of the injury are presented. Careful cleansing with soap and water in 82 of the cases was sufficient to prevent infection. In 35 cases followed to complete healing the average time required was 7.8 days.

Three of 14 patients treated by cauterization with phenol and alcohol gave evidence of inflammation but the wounds did not suppurate.

In 2 cases of human bite of the hand in which primary closure of the wound was carried out in addition to cleansing with soap and water the wounds became infected and required hospitalization.

These data when compared with previous reports would suggest that careful washing of early human bites with soap and water is preferable to other forms of immediate treatment whether it be chemical or electrocautery or surgical excision.

I wish to thank Dr. Don M. Morrill, superintendent of the Detroit Receiving Hospital, and my colleagues in charge of the emergency room, Drs. A. Z. Howard, B. R. Richey, J. R. Brown, and A. Finch, for their co-operation in allowing me to see and treat the majority of these patients.

#### BIBLIOGRAPHY

1. BATES, WILLIAM. Electrocauterization in the treatment of human bites. *Ann Surg*, 1931, 93: 641.
2. DIMITZA, A. On bites. *Schweiz med Wchnschr*, 1933, 65: 505.
3. DUNN, E. P. Human bites. *Am J Surg*, 1937, 36: 44.
4. LOWRY, THOMAS MCGRAIN. The surgical treatment of human bites. *Ann Surg*, 1936, 104: 1103.
5. MASON, M. L., and KOCH, S. L. Human bite infections of the hand. *Surg, Gynec. & Obst*, 1930, 51: 591-625.
6. McMASTERS, PAUL E. Human bite infections. *Am J Surg*, 1939, 45: 60-65.
7. WELCH, CLAUDE E. Human bite infections of the hand. *New England J Med*, 1936, 215: 901.

# THE TREATMENT OF RUPTURE OF THE URETHRA ESPECIALLY WHEN ACCOMPANYING FRACTURES OF THE PELVIC BONES

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THE increasing hazards of civil life lead each year to an increasing number of severe accidents. Injuries to the urethra are no exception to this statement once relatively rare traumatic lesions, they are now seen with sufficient frequency to necessitate detailed consideration. This is particularly important inasmuch as urethral injuries are usually caused by fractures of the pelvic bones and by "straddle injuries" to the perineum, lesions which often bring patients to surgeons not especially concerned with conditions of the genito-urinary system. It seems appropriate, therefore to consider in a journal of general circulation a group of patients with rupture of the urethra at various levels and to discuss the treatment with particular reference to those lesions accompanying fractures of the pelvis.

This paper is based on a series of 21 instances of rupture of the urethra treated in the Peter Bent Brigham Hospital. Of these 21 cases 12 involved the bulbous urethra and 9 the membranous urethra. All 9 patients who sustained rupture of the membranous urethra suffered this injury as a result of fracture of the pelvis. They presented far more complicated problems in diagnosis and treatment than the other group. It is natural that in the literature on this subject there has been particular emphasis on the management of visceral injuries, which are more obvious but not always more significant than the injury to the urethra and to the pelvic bones. Attention has been directed primarily to immediate life-saving measures, and little has been said regarding the prolonged postoperative and convalescent care of these patients. There is especially lacking a consideration of the simultaneous treatment of injury of the urinary tract and fractures of the pelvic bones. In a group of 160 patients with fracture of the pelvis, there were 9 patients whose fractures were complicated by rupture of the membranous urethra, only 4 who had rupture of the bladder. In our experience patients with rupture of the

membranous urethra are extremely difficult to manage, both from the standpoint of control of infection and of maintenance of a satisfactory position of the pelvic girdle. Although we have made free use of the available literature on various phases of rupture of the urethra, our methods have been worked out largely independently according to the requirements of the individual case. The literature on the subject is cited in the references at the end of this paper. A detailed review seems out of place in the present communication.

Fractures of the pelvic bones which are likely to be accompanied by urethral injury are produced by various crushing forces. The mechanism of injury is the lateral compression of the pelvic girdle, which causes collapse of the pubic and ischial arches and often fracture of the sacrum as well. The fragments (Fig. 1) of pubic and ischial rami are displaced medially posteriorly and downward, tearing the triangular ligament and its enclosed structures, notably the membranous urethra, pudendal vessels, and the voluntary sphincteric muscle. Fragments of pubis or ischium may be driven into the bladder tearing its wall either anteriorly or inferiorly lateral to the trigone and usually outside the peritoneal sac. However intraperitoneal rupture of the fall bladder may occur as a result of the same forces that cause the fracture of the pelvis.

When a patient has sustained a crushing injury to the bony pelvis, the immediate problem is to determine the extent of internal injuries at the same time that energetic measures are being instituted to combat shock. The intense pain requires repeated administration of morphine provided there is no cranial injury. Temporary immobilization of the pelvis and extremities on a Bradford frame with the aid of bandages is imperative. Failure to do this increases shock. A support under the knees for slight flexion of the thighs lessens pain by relieving muscle spasm. Besides the usual chart of blood pressure pulse and respiratory rates, repeated hematocrit and specific gravity studies of the blood are helpful in guiding the administration of parenteral fluids. Investigation of the urinary tract should be de-

From the Department of Surgery of the Harvard Medical School and the Urological Service of the Peter Bent Brigham Hospital, Boston. Read before the New England Regional Fracture Committee of the American College of Surgeons, May 27, 1928.

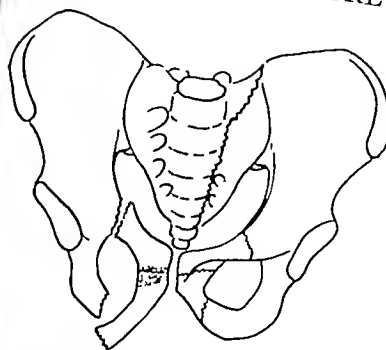


Fig 1 Roentgenogram of pelvis and diagram to show fractures of pubis, ischium, and sacrum caused by cave in of a gravel bank upon a man aged 23 years, which resulted in complete rupture of the membranous urethra and laceration of pudendal vessels. There was extensive retrovesical and retroperitoneal hemorrhage which extended up between the leaves of the mesentery and interfered with the circulation to the bowel. Abdominal exploration and suprapubic cystotomy were performed, and 11 months later plastic repair of the urethra was successful.

layed until the patient is seen by the surgeon who will have charge of his case. Enthusiastic instrumentation in the emergency room has often been misguided, and better evaluation is obtained after prompt transfer to the surgical ward.

Even in patients with fractures of the pelvis without injury to the urinary tract, inability to void at the time of admission is common since both shock and pain inhibit micturition. It may be difficult to elicit evidence of an injury to the urethra until some time has elapsed. The patient may have emptied the bladder a short time prior to the accident. It is also true that the hemoconcentration resulting from shock diminishes renal excretion. The presence of blood at the external urethral meatus contributes evidence of ruptured urethra.

After these preliminary considerations one may proceed with further details of examination. Intraperitoneal hemorrhage or urinary extravasation from rupture of the bladder causes diffuse abdominal tenderness and rigidity. The former is attended by signs of profound shock, which usually progresses rapidly and responds poorly to supportive measures. Extraperitoneal extravasation of blood and urine produces lower abdominal pain, tenderness, and muscle spasm. If the bladder is intact and the membranous urethra ruptured, the former may be palpated as a symmetrical rounded mass rising up out of the pelvis in the midline. When the bladder is ruptured, that organ will not be palpable. There may be, however, a mass in the suprapubic region or in an inguinal region as a result of extravascular urinary extravasation. A deformity of the pubic bone may be palpated, and gentle examination may elicit

crepitus. Tenderness over the sacro-iliac joints is due to the fracture itself, not to its complications. Paralyzes, anesthetics, paresthesias, and severe radiating pains in the extremities may result from injury of sacral nerve trunks. Careful rectal examination is of utmost importance in diagnosis. If the prostate gland is not palpable and the rectum is felt slightly com-

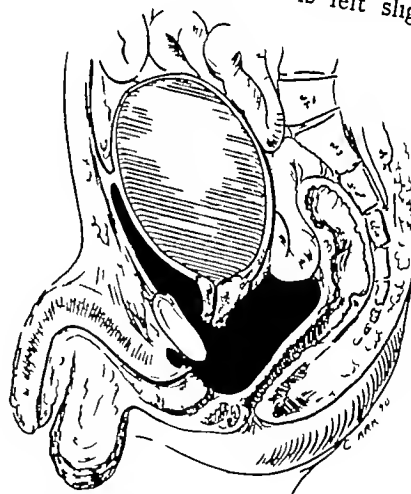


Fig 2 Diagrammatic sagittal section showing bladder and prostate separated as a unit from the urethra by laceration of its membranous portion and the urogenital diaphragm. Note the retrovesical hematoma and extravasation of blood and urine up into the prevesical space. The intrinsic vesical sphincter closes after such an injury and clear urine is usually found in the bladder at operation if that organ itself has not been injured. This diagram represents the findings at operation in 3 of our cases and is very similar to the condition described originally by Young.



Fig. 3. Roentgenogram of the pelvis of man aged 39 years made with the portable unit while shock was being combatted. The ind. filling urethral catheter does not reach the bladder but goes off to one side in the ischio-rectal fossa from which it drained 500 cubic centimeters of bloody fluid during the course of 4 hours. At operation the membranous urethra, as found to have been completely severed the bladder, as intact and contained 500 cubic centimeters of clear urine. Immediate restoration of the continuity of the urethra, as accomplished (see Fig. 5).

pressed by a soft mass in the pelvis, a complete rupture of the membranous urethra is certain. It indicates that the prostate and bladder have been torn from their attachments and displaced upward as a unit by the retrovesical hematoma (Fig. 3).

Hemorrhage and urinary extravasation may cause both swelling and discoloration of the perineum. The location and nature of such extravasations is of considerable diagnostic importance. At times these signs do not appear for several hours, and repeated examination must be made for them. Following rupture of the membranous urethra the perineal mass appears later and is likely to become diffuse. If the swelling and discoloration appear immediately and are confined wholly or in large part to one side of the perineum the rupture has probably occurred in the bulbous rather than the membranous urethra. The presence of a mass in the suprapubic region or inguinal region indicates either a rupture of the membranous urethra and urogenital diaphragm or of the anterior wall of the bladder. When the two layers of the urogenital diaphragm are torn, hemorrhage from the pudendal vessels and urine from the urethra is permitted to escape freely into the perineal tissues, periprostatic spaces, and directly up into the prevesical space.

A catheter may be passed, but complete urological investigation is not necessary in every patient who cannot void after an accident, especially in the presence of negative roentgenogram as



Fig. 4. Roentgenogram of pelvis and hips of man aged 45 years, who fell distance of 40 feet landing on his left side. There are fractures of left pubis, ilium, ischium, and neck of the femur. There is no visible displacement that could injure urethra or bladder. One can discern symmetrical rounded shadow in the pelvis which is probably full bladder. The patient, as not catheterized, and 6 hours after injury of or relief of pain and shock, he voided 500 cubic centimeters of normal urine.

will be discussed. If the catheter seems to be in the bladder it should be left in place for the present. In general irrigation should be cautiously avoided. Keyes mentions it only in condemnation, and our experience confirms this teaching. At times it may be justifiable gently to irrigate the catheter with about an ounce of saline or boric acid solution in order to insure its patency and freedom from obstruction by clotted blood. There may be difficulty interpreting observations made during the passage of the catheter since it is sometimes uncertain whether the catheter is actually in the bladder and also whether the primary injury is to the bladder or urethra. It is usually impossible to pass a catheter into the bladder when the membranous urethra is ruptured. In this case the catheter may pass into the prevesical space or ischio-rectal fossa. Withdrawal of bloody fluid may lead the surgeon to believe that not only is the catheter in the bladder but that the bladder itself is ruptured. In the passage of the catheter it must always be remembered that a partial rupture of either the bladder or the urethra may be converted into complete rupture by careless or unduly forceful instrumentation.

Powers and Smith have emphasized the value of suprapubic cystostomy and retrograde instrumentation of the urethra. They used the latter maneuver to discover whether the instruments passed through the urethra emerged through the internal orifice or whether they passed off into a false passage before reaching the bladder. They

# HARRISON THE TREATMENT OF RUPTURE OF THE URETHRA

suggest removing the urethral tube in 12 to 14 days and leaving a filiform in place to act as a splint. The length of time suitable to have the urethral catheter in place is arbitrary and varies in different cases. We have left such a tube in place as long as 6 weeks. Also, we use the urethral catheter as a source of drainage of the bladder and believe that this protects the site of rupture from urinary leakage. If the catheter causes a purulent urethritis and systemic reaction, it should be immediately removed, and a silk thread attached to the abdominal wall, left in the urethra, to act as a splint.

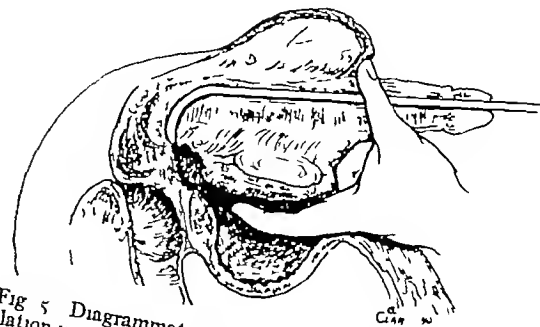


Fig 5 Diagrammatic representation of operative manipulation in which the right index finger is passing into the bladder outlet in order to thread it over the end of sound in the distal end of ruptured portion of urethra

A portable roentgenogram of the pelvis is of great importance in determining the extent and character of the injury. It serves to indicate not only the type of fracture present, but also whether the catheter, previously inserted, follows the course of the urethra into the bladder or whether it veers into the perineum as happened in one of our cases (Fig 3). In determining the position of the catheter, the surgeon may correlate these findings with rectal palpation. The roentgenogram may give valuable aid in ruling out rupture of the urethra, for it may show multiple fractures of the pelvis without such displacement of any fragment as to cause injury of either urethra or bladder. Also, such a film may show the rounded symmetrical shadow of an intact full bladder (Fig 4). Expectant treatment in such cases is desirable and voiding will often take place normally once immobilization of the pelvis and extremities. The once prevalent teaching, that every such patient should be immediately catheterized, is not now tenable.

Cystoscopic examination of patients who have sustained violent trauma is obviously contraindicated. Immediate excretory urography is not an appropriate procedure for the patient in shock but may be helpful later, particularly when renal injury is suspected in addition to the trauma to the urinary passages. The use of the urethrogram should be delayed usually for 3 to 6 weeks after trauma. At the end of that interval it is advisable to use this method to determine the state of the urethra after regeneration has taken place. It is conceivable that rupture of the urethra may be ruled out early in mild doubtful cases by means of this procedure.

For rupture of the urethra at or above the triangular ligament, suprapubic cystotomy should invariably be performed. At operation all blood and urine are aspirated from the prevesical space. The bony fragments are elevated from the lacerated urethra. Simultaneous manipulation of the

lower extremities by an assistant may facilitate this maneuver. The bladder is opened and examined for evidence of injury. A sound is passed through the penile urethra and guided in its passage to the displaced prostatic urethra by the index finger of the right hand placed in the orifice of the vesical outlet (Fig 5). The end of a catheter is inserted over the end of the sound in the bladder and drawn in a retrograde manner through the urethra, thus re-establishing its continuity. A silk suture is passed through the proximal end of the catheter in the bladder and its end attached to the abdominal wall. A drain is left in the prevesical space and the bladder closed with a de Pezzer catheter in place. The patient's legs are then flexed in slight abduction and perineal section performed quickly to establish drainage of blood and urine accumulated in the perineum.

Immediately after operation the patient should be immobilized on a Bradford frame and the region of the sacrum and buttocks protected by a sponge rubber pad. Further immobilization of the pelvis and more satisfactory alignment of the fragments of the bones may be obtained by a Russell type of traction applied to both legs. By regulating the weights for traction on each extremity according to the deformity present, structural defects can be corrected and further distortion prevented. This method permits support of the thighs and longitudinal traction simultaneously, thus allowing the extremities to swing free without exerting an undesirable drag on the pelvis. The excellent results obtained by this method of treatment are well shown in Figure 6. In several days, as soon as the patient's general condition permits, anterior and posterior body shells of plaster should be made to allow turning to avoid decubitus ulcer. Prevesical drainage is facilitated when the patient is placed so that he is lying on

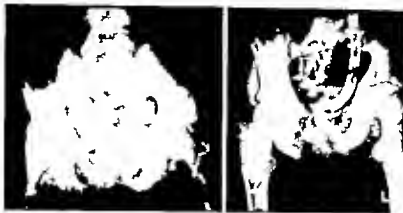


Fig. 6 (left). Roentgenogram of pelvis 3 months after fractures of pubis, ischia, and sacrum accompanied by rupture of urethra. Note only slight narrowing of pelvis and good horizontal alignment of acetabular and iliac crests. The patient obtained also an excellent functional result and as a sliding rib support of crutches 1 this time. Contrast with Figure 7.

Fig. 7. Roentgenogram of the pelvis 3 months after fractures of the pelvis which originally appeared as in Figure 1. Note the undesirable results, namely: narrow, heart-shaped pelvis, poor alignment of level of acetabula and ilia, medial collapse of pubic arch, and rotation of entire right side of pelvis. The functional result is not good, the patient walks with difficulty; there is marked gait abnormality, and he suffers constantly with low back pain. This is a common result from use of the pelvic sling. Contrast with Figure 6.

his abdomen. However extreme edema of the penis and scrotum may be anticipated if the patient is left in this position more than a few hours. Frequent change of position is required if the edema becomes severe. Physiotherapy is imperative early in the course of treatment to lessen muscle atrophy. The prevention of permanent abnormality of gait and posture is a major consideration sometimes overlooked in the early care of these patients. We have not obtained good results with the pelvic sling. Patients treated in this way are often left with a narrow "heart-shaped" pelvis which causes more disability than is the case when the pelvis is too wide (Fig. 7). Fragments of pubic bones may become infected and are sometimes extruded spontaneously.

Decubitus ulcer is a common complication that assumes grave importance if not anticipated and treated promptly. For a completely successful result these complications must be prevented by early recognition and treatment at the same time that restoration of the urinary tract is under taken.

At an appropriate time several weeks after operation the urethral catheter is removed. The suture attached to its vesical end is drawn down through the urethra, and its other end is left attached to the abdominal wall by way of the bladder and suprapubic sinus. The urethra is

then filled with radio-opaque material and an exposure is made with the portable roentgenographic unit (Fig. 8). If there is no extravasation of the opaque fluid the catheter is not replaced, but the silk thread is retained as a guide for the passage of instruments. When the surgeon is certain that the urethra is healed and has an adequate lumen, the suprapubic catheter may be removed; the fistula is allowed to close, and neostomy then takes place through the urethra. At this time there is the greatest danger of the appearance of acute pyelonephritis as a complication. Frequent cultures of the urine are made and appropriate chemotherapy instituted if infection is detected. Calibration of the urethra is carried out twice a week; dilatation is made slowly in order to minimize the extent of periurethral fibrosis. The development of some degree of urethral stricture is inevitable in all of these patients. Post-traumatic strictures are more difficult to manage than those of infectious or congenital origin. The degree of constriction may vary but in any event must be checked at intervals throughout the rest of the patient's lives. A serious predicament results when they are neglected and allowed to contract. This is well illustrated in Figure 9, a urethrogram of a patient who, after 3 years of successful treatment, allowed his condition to be neglected for 3 years. It is now impossible to ob-



Fig 8, left Roentgenogram of pelvis, urethra being filled with skioldan 6 weeks after complete rupture as shown in Figure 2. Complete regeneration has occurred, and there is no evidence of extravasation. The opaque fluid has passed into the bladder. A suprapubic catheter remains in place in the bladder.

Fig 9 Roentgenogram of pelvis and urethrogram on patient 20 years after fractures of pelvis and rupture of urethra. Neglect of dilatation of urethra for 3 years has resulted in dense stricture that markedly narrows lumen of posterior urethra. Note fragments of bone displaced down into thigh. The small, round, opaque shadows in the pelvis lie outside of the urinary tract and are probably phleboliths.

tain a urethral lumen larger than No. 18 French in this patient, and even this can be maintained only by frequent dilatation. He has a considerable degree of hydronephrosis and hydro-ureter as a result of the long neglect. Technically, a surgeon undertaking the dilatation of a stricture resulting from trauma must use extreme caution and delicacy in his manipulation. The patient's reaction is an excellent index of the efficiency of instrumentation. If instrumentation is painful, he will not return, and, if he is wise, will go elsewhere for treatment. The slightest sign of blood also is a danger signal, compelling cessation of treatment for that day. Distention of the urethra with a lubricant such as mineral oil, or a mixture of nupercaine and lubricating jelly prior to instrumentation greatly facilitates the passage of instruments.

The seriousness of rupture of the membranous urethra is emphasized by the end-results in a series like the present. In this series, patients have been under the care of the genito-urinary surgeon from the time of admission to the hospital, yet the results, especially when entrance to the hospital has been delayed, have not been brilliant. Two of the patients who sustained rupture of the membranous urethra died on the day of injury as a result of shock from extensive internal injuries. It is apparent in retrospect that in

neither instance was shock combatted adequately according to the modern concept of treatment. Three of the patients having rupture of the bladder died within 1 week as a result of extensive injuries and infection. The other patient, a woman aged 69 years, died 2 months later of bronchopneumonia and renal sepsis. Suprapubic cystotomy and suture of the vesical rupture were carried out in each of these cases, but only one was brought to the hospital on the day of injury. A mortality rate as low as 20 per cent has been reported for those cases in which treatment began within 12 hours after injury. After that period of delay, however, the mortality leaps to 85 to 90 per cent.

Four of the patients having rupture of the membranous urethra were treated by combined suprapubic cystotomy and perineal drainage. In one instance the continuity of the urethra was immediately restored. In another, suprapubic cystotomy was performed initially and 1 month later successful anastomosis of the urethra was made. Suprapubic cystotomy and perineal drainage were established in 2 patients, plastic repair of the urethra was performed 8 and 11 months later, respectively. In another case, a boy aged 7, cystotomy was performed in another hospital and urethroplasty attempted here 9 months later without success (Fig 10). There was a mass of





Fig. 1, left. Oblique urethrogram of boy aged 6 who had sustained complete rupture of the membranous urethra and fracture of the pelvis 9 months previously. Note the extreme irregularity of the canal and particularly the obliteration of the channel at the canal junction. The false passages are apparent, probably occurring from instrumentation. Attempts at plastic repair were unsuccessful owing to dense cicatricial tissue.

Fig. 1, right. Intravenous urogram 7 years after ureteral transplantation into the bowel and total cystectomy. The patient is quite well 6 years later.

cicatricial than 5 centimeters in thickness between the urethra and bladder. Two operative attempts to establish a patent canal through to the bladder were unsuccessful. This patient illustrates the error of suprapubic drainage without immediate regard for restoring the continuity of the urethra, or perineal drainage if this is impossible. Finally ureteral transplantation into the bowel and total cystectomy were performed. The patient is entirely well today, 6 years later (Fig. 1). The results (Fig. 2) in these cases show that original perineal drainage diminishes the hazard of infection and proliferation of fibrous tissue which so often makes subsequent attempts at plastic repair of the urethra almost impossible. If initial restoration of the continuity of the urethra by catheter or suture is possible, secondary operation is avoided altogether.

The results at other clinics emphasize, as do our own, the seriousness of these injuries. A series of 30 instances of rupture of the urethra were reported from the Massachusetts General Hospital by Smith and Mintz. Thirteen of these were sustained in conjunction with fractures of the pelvis; 9 of these patients died. In 3 cases, death occurred within 24 hours as a result of shock and other injuries. Three patients died much later as a result of sepsis in and about the urinary tract. The 3 others died later of complications not directly related to the urinary tract. Of the 4 patients who lived, 1 had no operation but was drained by urethral catheter for 16 days; re-

covery ensued in another 31 days after suprapubic cystotomy and retrograde catheterization; 1 patient was successfully treated by combined cystotomy and perineal section; only cystotomy was performed for 1 patient who was discharged from the hospital bearing a suprapubic tube 7 weeks later. There were 7 patients having rupture of the bulbous urethra without fracture of the pelvis, only 1 of whom died.

Culver reported a mortality of 2 per cent in a series of 18 patients having fractured pelvis and ruptured urethra. Fourteen patients with straddle injuries as the cause of rupture of the urethra all recovered. External urethrotomy was performed in 10 cases, combined in 7 with suprapubic cystotomy and retrograde catheterization of the bladder. Four patients were treated conservatively with good results. His experience showed that, after hemorrhage and urinary retention have been cared for, local sepsis in the perineum causes longstanding urinary fistula and subsequent stricture formation. Proper early surgical management minimizes local infection. Three patients had long periods of hospitalization and some permanent impairment of function because of failure to restore the continuity of the urethra at the same time that suprapubic cystotomy was performed. Later management of these patients consisted of measures to combat urinary infection and to dilate the urethra. It was pointed out that straddle injuries usually occur below the urogenital diaphragm and require



Fig 12 Anteroposterior and lateral views Combined urethrogram and cystogram made 3 months after fracture of pelvis and rupture of urethra showing wide separation of proximal end of urethra and bladder outlet Dense cicatricial tissue has obliterated the posterior urethra as result of failure to restore its continuity at the time of cystostomy The impingement of the displaced fragments of the pubis and ischium on the position of the posterior urethra is graphically shown Successful anastomosis of urethra to bladder was made 11 months after injury

only perineal operation Urethral injuries by pelvic fracture occur in and above the diaphragm and require suprapubic operation We agree with this opinion but feel that, in addition, perineal drainage in these cases lessens local sepsis A satisfactory lithotomy position is difficult to obtain and unwise for a patient who has recently sustained fracture of the pelvis This we believe to be a contra-indication to primary suture of the urethra by way of the perineum in most cases of fracture of the pelvis Young has accomplished the brilliant feat of successfully performing this operation on one patient in the home

This paper has thus far discussed the symptoms and treatment of ruptures of the membranous urethra, especially those accompanying fractures of the pelvic bones Many of the considerations in regard to treatment, however, such as those concerning stricture as a result of the rupture of the urethra, are applicable to injuries at any level of this passage

In the present series of 21 instances of rupture of the urethra, there were 12 cases in which the lesion was in the bulbous urethra as against 9 in the membranous portion Rupture of the bulbous urethra is usually a less serious condition than a corresponding injury to the membranous urethra This is shown not only in the present series but also by other series in the literature, such as that of Smith and Mintz As suggested by the ana-

tomical location, the bulbous urethra is usually ruptured, not as the result of fracture of the pelvic bones, but from a variety of sources of trauma Such injuries may be the result of falls astride sharp objects (4 patients in our series), faulty instrumentation of the urethra by the surgeon (3 instances), and also self-inflicted injury as the result of insertion of foreign bodies in the urethra (5 patients)

Three of the patients having rupture of the bulbous urethra received drainage of the bladder by means of a urethral catheter Later, incision and drainage of peri-urethral abscess was necessary in 2 of these cases Each of the 3 patients was in the hospital for 14 days, and since then regular treatment for urethral stricture has been necessary External urethrotomy was performed upon 3 patients in this group Two were well 2 weeks after injury, and 1 died the day after operation The latter patient, a man aged 52 years, suffered an instrumental perforation of the urethra 1 week before admission to the hospital In 6 days urinary extravasation and infection had caused gangrene of the perineum Also there was noted total retention of urine when he was first seen Immediate perineal drainage was established, and death took place within 36 hours This case is a good illustration of the grave consequences which follow neglect of the presence of extravasated urine



Fig. 3. left. Roentgenogram of the pelvis showing the shadow of glass stirring rod which was introduced into the urethra and spontaneously passed into the bladder. Its distal end was buried in the urethral bulb and was palpable in the perineum.

Fig. 4. Urethrogram 2 weeks after urethrotomy to remove stirring rod from urethra and bladder. This shows the promptness of healing without stricture when the urethra is opened and closed surgically in the absence of urinary extravasation.

Five injuries of the bulbous and penile urethra by foreign bodies have been treated. There was perforation of the urethra by sharp hair pins in 2 cases. Two sharp pointed pencils and glass stirring rod, found in the 3 other patients, were so imbedded in the mucous membrane of the bulbous urethra that removal without operation was impossible. External urethrotomy was performed in each instance, and the successful removal of the intact foreign body accomplished. The pencils and the stirring rod (Fig. 3) had each passed into the bladder and the distal end of each could be palpated at the point of protrusion into the urethral bulb. One patient whose urethra was perforated by a hair pin developed a peri-urethral abscess. A primary closure of the urethra was made in the 4 other cases, and urination was normal at the end of 1 week. An indwelling urethral catheter was required after operation in only 1 of these patients. His temperature rose to 104 degrees the day after operation but returned to normal in 3 days; the catheter was removed after 6 days. The perineal wound healed by primary intention, and a urethrogram 2 weeks later showed no evidence of stricture (Fig. 4). At the end of 2 months no stricture was found when the urethra was calibrated.

If it is determined that a patient has a rupture of the bulbous urethra, immediate perineal section is indicated for control of hemorrhage and urinary extravasation. The use of an indwelling urethral catheter alone will not usually suffice as peri-urethral abscess will always develop in the

presence of urine in the tissues outside the urethra, because extra-urination interferes with local circulation and causes necrosis and infection. Primary closure of the urethra over an indwelling catheter may be carried out but not without increasing the hazard of infection. It is our experience that an external urethrotomy wound that is left open to drain freely will heal quickly once infection in the perineal tissues is controlled. This method has the merit of safety without unduly prolonged hospitalization.

#### SUMMARY

The methods used in the treatment of patients having injury of the urethra have been presented. Twelve of these had injury of the bulbous urethra. Nine patients had rupture of the membranous urethra as a result of fractures of the pelvic bones.

Certain points in physical examination and roentgenographic findings that are diagnostic aids have been described. The best results for rupture of the bulbous urethra have been obtained by immediate external urethrotomy whereas the operative management of rupture of the membranous urethra consists of a combined suprapubic and perineal approach, particularly when accompanied by fracture of the pubis and ischium. The important details of simultaneous treatment of the fractures of the pelvic bones have been emphasized. The methods that we have found to give the best results in each type of injury have been outlined.

## BIBLIOGRAPHY

- 1 CROSBIE, A H Rupture of the urinary bladder  
J Urol, 1924, 22 431
- 2 CULVER, HARRY Traumatic rupture of male urethra  
Illinois Med J, 1938, 74 500-506
- 3 EWELL, G H The value of excretion urography in  
traumatic injuries of the urinary tract. Urol &  
Cutan Rev, 1935, 39 No 10
- 4 FOULDS, G S Traumatic rupture of the urethra and  
bladder Canadian M Ass J, 1930, 22 365
- 5 GORDON TAYLOR, GORDON Complicated injuries of  
the urinary tract Brit. J Urol, 1940, 12 1
- 6 McWHORTER G L Use of the seton in repair of torn  
or strictured urethra Surg, Gynec & Obst, 1937,  
40 247
- 7 POWERS, J H, and SMITH, D W The treatment of  
traumatic rupture of the posterior urethra New  
York St J Med, 1932, Oct. 15
- 8 SMITH, C G, and MINTZ, E R. Rupture of the  
male urethra New England J Med, 1931, 205  
No 9
- 9 STIRLING, W CALHOUN Traumatic rupture of the  
bladder and urethra J Urol, 1927, 17 503
- 10 STIRLING, W CALHOUN, and BELT, N Traumatic  
rupture of the bladder with perivesical extravasa-  
tion J Am. M Ass, 1929, 92 2006
- 11 YOUNG, H H Wounds of the Genito-urinary Tract  
US Government Printing Office, 1927
- 12 Idem Treatment of complete rupture of the posterior  
urethra, recent or ancient, by anastomosis Tr Am  
Ass Gen-Urin Surg, 1928, 21 405

# TRANSUMBILICAL REPAIR OF CONGENITAL UMBILICAL HERNIA

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**A**n operative technique is described for the repair of umbilical hernia in children without the production of a noticeable defect.

Small congenital umbilical hernias usually disappear before the age of 3 years. This may occur spontaneously or with the assistance of abdominal strapping. The condition is usually asymptomatic although the child may complain of fleeting periumbilical pains. The complaint of the parent is that the unsightly bulge involving the umbilicus has not diminished or may be increasing in size. The operation for which this technique is applicable is done only when the hernia is increasing in size or is giving symptoms.

## REQUIREMENTS OF OPERATION

The surgical repair of congenital umbilical hernia requires the excision of the hernial sac and closure of the fascial ring. It seemed desirable to do this with an inconspicuous scar. An attempt was made, therefore, to carry out the repair by means of a *transumbilical* approach so planned that at the end of the procedure the scar would fall within the cutaneous ring of the umbilicus itself and therefore would be essentially invisible. Fourteen patients have been operated upon with this technique at the Children's Hospital. We have found that the fascial ring can be well closed and that the recti may be united for several centimeters above and below the umbilicus and that the postoperative result is satisfactory.

## OPERATIVE PROCEDURE

The umbilicus is cleansed with soap and water prior to the application of the usual skin antiseptic. A "weak" Allis clamp or small double hook is placed on the central portion of the umbilical skin for traction. The umbilicus is everted, and the line of incision is scratched or marked with dye on the skin of the upper portion of the hernia. The scratch is made as a convex upward semicircle so arranged that as the umbilicus is inverted, the mark lies just within the umbilical cutaneous ring (Fig. 1). The upper portion of the umbilical skin is chosen for incision to allow

easier access for closure of the diastasis recti which is more commonly found above than below the hernial ring. The umbilicus is everted and the skin incised with a small blade down to the cleavage plane between the skin and the fascial covering of the hernial sac. Over the sac and in the region of the diastasis there is very little fat in the areolar tissue of this plane. The plane is developed by scissors dissection upward along the surface of the inter-rectus fascia and laterally as far as the medial edges of the rectus muscles. In this manner the hernial sac becomes apparent. The dissection should be kept close to the inter-rectus fascia to prevent cutting into the vascular fatty panniculus overlying the anterior rectus fascia. Development of the rectus fascia below the hernia is permitted by cutting off the top of the sac, which is attached to the central portion of the umbilical skin. The plane between the skin and superficial fascia investing the inferior surface of the sac is thus opened for dissection (Fig. 2, a to e). The Allis clamp may now be removed and the skin flap of the umbilicus folded back out of the field.

Hemostats are applied to the margins of the open sac for traction. The anterior rectus fascia should be cleared for 3 or 4 millimeters lateral to the medial edges of the rectus muscles upward and downward to the point where the rectus muscles meet in the midline. The skin incision may be displaced by proper retraction to facilitate the dissection. It is important to locate the position of the medial edges of the rectus muscles beneath the fascia so that they may be properly brought together in the midline. The medial edges of the muscles beneath the anterior rectus fascia are identified (1) by the somewhat gray color imparted to the anterior fascia by the muscle tissue beneath (2) by the perforating vessels which appear through the anterior fascia approximately to the medial edges of the muscles just above and below the umbilicus (3) by the appearance of the edges of the recti, which on elevation and depression of the inter-rectus fascia seem to be relatively tense lateral bands in the loose inter-rectus fascia. After the fascia has been thoroughly exposed, the hernial sac is trimmed off to leave a collar of about 3 to 4 millimeters in width. The neck of the

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Fig. 2. Pre-operative and postoperative photographs of moderate-sized umbilical hernia in two year old child.



Fig. 3. Pre-operative and postoperative photographs of relatively large umbilical hernia in two year old child.

fragment of peritoneum is removed to preclude the possibility of fluid being secreted by peritoneal tissue buried beneath the umbilicus (Fig. 4m). The umbilical skin is anchored to either side of the midline fascial approximation by two to four silk sutures so placed as to insure proper reposition of the umbilicus. Fine interrupted silk sutures are used to unite the skin edges. It is found that when the umbilicus has been attached to the fascia, the skin incision is inverted within the umbilical cutaneous ring.

A small roll of gauze is placed in the depression of the umbilicus to maintain the shape of the umbilicus and to promote adhesion of the umbilical skin to the fascia. A dry sterile dressing with wide adhesive tapes is applied. The sutures may be removed at the usual time without difficulty.

Among 14 patients who have been operated upon with this technique there have been no wound infections or postoperative complications. Postoperative examinations have been made on the first 8 cases, 3 to 6 months following this procedure. The results have been entirely satisfactory. Figures 2 and 3 show the preoperative and postoperative appearance of representative cases of umbilical hernias treated with this procedure.

#### SUMMARY

A technique has been presented for the repair of umbilical hernia in childhood. This procedure has been employed on 14 patients at the Children's Hospital. In each instance it has resulted in a satisfactory cure with a normal appearing umbilicus and an inconspicuous scar.

## CARCINOMA ERYSIPELATODES

### Subepidermal Lymphatic Metastases Confused with Operative Sequelae

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**S**KIN metastases from carcinoma of the breast may be so disguised as to be mistaken for postoperative inflammatory entities. A group referred to as having erysipelas-like characteristics is seldom identified correctly when first seen. The origin may be in the neighborhood of a mastectomy scar, and is marked by reddening and some edema of the skin, with a flaming, well demarcated, advancing border. Histologically, the skin appears free from pathology except for metastatic permeation of the subpapillary vessels. There is no final agreement as to whether these vessels are capillaries or lymphatics. We have studied two typical cases, both of which were mistaken for postoperative complications. They were treated as such for some months before the correct diagnosis was made. Available biopsy material subjected to serial sectioning clarified some mooted points.

The resemblance of certain metastatic lesions to erysipelas was noted by Unna. It was not until 1924, however, that the condition was given a specific name. Kuettner, describing such a disorder, called it "erysipelas carcinomatosa." He believed the metastatic process involved the superficial blood vessels. In the same year, Lee and Tannenbaum reported 28 cases of what they called "inflammatory carcinoma" of the breast, some of which resembled erysipelas and undoubtedly fall into this group. In spite of the wide variations in the pathological findings of the primary neoplasm, the inflammatory aspect was considered a distinct clinical phase, with diffuse lymphatic metastases as the most manifest pathological feature. Venues, likewise, were thought to be involved. In 1928 Ruder differentiated the condition from Paget's disease by its subepidermal rather than its intra-epidermal metastatic extension. He called the involved channels blood vessels. Rasch in 1931 considered the name "erysipelas carcinomatosa" unfortunate, since the condition is primarily cancerous. He therefore proposed the name "carcinoma erysipelatodes," and differentiated it from cancer encuirasse as

did Kuettner, by its lack of scleroderma-like skin and by its propagation in what he felt were blood vessels. Barber presented a case of Paget's disease which had an erysipelas-like discoloration of the chest wall. The metastatic propagation was thought to be in blood vessels. In 1933 Weber (13) chose the name "telangiectatic carcinoma," because a case noted by him did not resemble erysipelas. Sections taken from a spreading area revealed an enormous dilatation of what were apparently cutaneous capillaries, in which were found cancer cells. Some of the vessels which did not contain red cells might have been lymphatics. Shortly afterward, von Vonno described a similar case as "carcinoma telangiectaticum." Weber (14) believed that the condition deserved a special niche in clinical medicine, and that it could be found in association with Paget's disease or cancer encuirasse. He stated that it spread mainly by way of blood vessels, although lymphatics and tissue spaces could be involved.

On the other hand, Pfahler and Case described the process as extending largely through the lymphatics and only rarely through blood vessels. They had noted and indexed 15 cases as "malignant lymphangitis," but changed the name to "erysipelas carcinomatosa" to conform with those previously reported in the literature. They emphasized the frequency with which it was mistaken for radiodermatitis or radiotelangiectasis. Case discussed the histopathological picture as being similar to that reported in the literature, with the exception that the marked capillary dilatation and predominance of blood vessel invasion were not found. The malignant cells appeared in the lymphatics or tissue spaces. This, he stated, was in agreement with the findings of many investigators, including Fischer, Brackertz, Mandl, Durst, Delbanco, Cemjachowsky, and Bondarcuk (3) who were of the opinion that the tumor cells spread by way of the lymphatics. Rotter studied 4 cases, 1 of which was in a male. After careful histological scrutiny he decided that only lymphatics were involved. Freeman and Lynch described a patient, who, 1 year after surgery for breast malignancy, developed an eruption which might have been mistaken for lymphoheman-

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Fig. 2, left: Case 1—arm first seen. Not the small enlargement just above the arrow and the large axillary metastases. No inflammatory elements are present.

Fig. 2, right: Case 1—30 months after mastectomy. The skin presented flaming red, clearly margined eruption which spread in all directions from the mastectomy scar. The well-demarcated posterior edge may be seen.

gioma. Few characteristics of erysipelas were present. Microscopically there were unidentified vascular channels crowded with tumor cells. The presence of erythrocytes in some suggested that at least an occasional blood vessel was involved along with the lymphatic vessels. The authors question whether in the absence of redness, elevation of temperature and active spreading border

one should call the disorder carcinoma erysipeloides. When diffuse cutaneous infiltration is an outstanding feature, they prefer the term *solid epidermal carcinoma*. Sateenstem recalled case in which the extension was by both blood vessels and lymphatics. Dawson and Shaw reported bilateral breast neoplasm which extended to distant organs by way of lymphatic and blood channels.



Fig. 3: Biopsy of skin lesion of Case 1. This thin-walled vessel containing tumor cells.



Fig. 4: Erythrocytes.



Fig 5

Fig 5 Case 2, on admission. An elevated hard mass, covered by red, glossy skin, was present with metastases at the right pectoral border. No inflammatory elements were noted.



Fig 6

Fig 6 Case 2, 5 months after operation. A brownish red, well-demarcated discoloration extended medially from the mastectomy scar. Biopsy specimens were taken from the middle and edge of the lesion.



Fig 8

Fig 8 Case 2, 9 months after operation. A red mottling had appeared on the opposite breast.

sels. Dilatation of channels was a prominent feature. They therefore felt justified in describing the disorder as "generalized telangiectatic carcinoma." They suggest that carcinoma erysipelatodes is merely a late stage of malignant mammary tumor with cutaneous carcinomatosis which may in some cases be associated with more typical forms of cancer en cuirasse and Paget's disease of the nipple. They felt there was little justification for regarding this, when accompanied by reddening, a distinct pathological entity as suggested by a specific name.

The great variance in the foregoing reports indicates a need for additional study of the underlying process. Two patients with carcinoma of the breast, who, after operation, presented clinical features suggesting erysipelas, were observed. The skin was studied by repeated biopsy in an effort to clarify some of the pathological features. This material was sectioned serially.

#### REPORT OF CASES

CASE 1. C. S., a white American female, aged 47 years, entered the Brooklyn Cancer Institute on March 2, 1936, with a chief complaint of an enlarged gland in the right armpit of 1 year's duration. She had had no knowledge of a mass in the breast. Her family and past histories were irrelevant. Physical examination revealed both breasts to be small, with practically no glandular tissue palpable. A 2.5 centimeter nodule, not attached to the skin or chest wall, was palpated above and external to the areola of the right breast. Associated with this were matted glands in the midaxillary and anterior axillary fold on the same

side, approximately 3 times larger than the primary lesion. The glands were freely mobile. No other regional or distant metastases and no inflammatory aspects were noted (Fig 1).

She was given roentgen therapy and the following factors were used: 200 kilovolt, 40 centimeter skin, target distance, 1 millimeter of copper and 1 millimeter aluminum filtration, two 6 by 8 centimeter fields, anterior and lateral ports cross-firing the breast and areola, for a total of 1600 r each. The same factors were used via 1 anterior and 1 posterior 10 by 15 centimeter portal to the axilla for a total of 1600 r to each. Following roentgen therapy, there was marked diminution in the notable pathology



Fig 7. Section of skin lesion from Case 2. Subpapillary channels are slightly distended with masses of tumor cells.



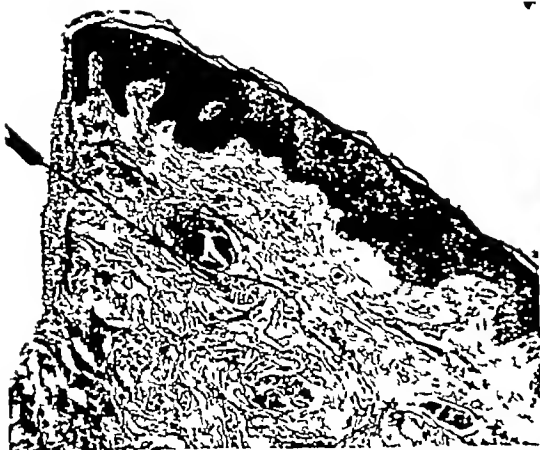


Fig 12 At this magnification a group of tumor cells appear to lie in a blood vessel containing erythrocytes

Eight months previous to admission, she noticed a walnut sized, hard, painless mass in the right breast which grew larger slowly. The skin became involved 6 months after the appearance of the mass.

Physical examination revealed an elevated, round, hard, 4 centimeter mass situated in the upper outer quadrant of the right breast, covered by a red, glossy skin. In the right pectoral border, a 5 centimeter sized indurated, metastasis was found, adherent to the skin. The supraclavicular area was negative (Fig 5). Laboratory examination including roentgenograms of the chest revealed no evidence of distant metastases. Wassermann was negative. Urine and blood tests showed them to be normal. Specimen obtained by punch biopsy of the breast was reported as carcinoma.

She received a course of pre-operative roentgen therapy between May 31, 1938, and July 13, 1938. The following factors were used: 200 kilovolt, 50 centimeter skin, target distance, 2 millimeters copper and 1 millimeter aluminum filtration, 2 ports cross-firing each of the areas treated, breast ports 10 by 15 centimeters, other ports 8 by 10 centimeters. The breast received 3,000 r to each port with a tumor dose of 3,030 r. The axilla received 2,600 r to each port with a tumor dose of 3,926 r. The right supraclavicular region received 2,400 r to 2 ports with a tumor dose of 3,878 r. A satisfactory radiation reaction was noted on the skin. The breast mass broke through the skin following therapy but this healed following conservative treatment. The mass in the axilla diminished in size and was softer.

On October 1, 1938, a radical mastectomy was performed. Involved glands had to be dissected away from the axillary vein and from the lateral border of the latissimus dorsi. A large skin flap was removed from the breast, necessitating the undermining of the skin toward the midline of the sternum and also at the lateral border of the incision.

**Pathology** A 4 centimeter mass was present in the upper outer quadrant, adherent to the skin. Several axillary glands appeared to be grossly involved in the neoplastic process. Sections through the mass were composed of an extremely dense, poorly cellular, fibrous tissue within which were numerous small rows of neoplastic cells which for the most part showed no definable cell bodies, and irregular, extremely chromatic nuclei. Vesicular nuclei were rare. Nucleoli and mitoses were absent. There was a very scant lymphocytic infiltrate. Groups of tumor cells



Fig 13 High magnification of tumor cells seen in Figure 12. They are confined to a lymphatic which is surrounded by the branching of a capillary. Arrow points to the single cell thickness of their respective walls. The erythrocytes are confined to the capillary.

which extended into the surrounding fatty tissue showed less change, the nuclei commonly being vesicular. An axillary lymph node was almost completely replaced by tumor tissue which showed a distinct alveolar and sometimes a pseudoglandular arrangement, the individual cells being prominent, with a pale cytoplasm, vesicular nuclei, and distinctly definable nucleoli. No mitotic figures were noted. No findings of note were present in the sections through the nipple, skin, or underlying large ducts or lobules. There was no involvement of the underlying pectoral muscle. The diagnosis was duct carcinoma of breast, with axillary lymph node metastases, marked radiation changes in the breast mass.

The wound healed uneventfully except for a small triangular area at its center, which was treated with azochloramide solution and later with cod liver oil ointment. One month after operation, marked erythema was noted extending medially from the wound. The patient stated that the reddening followed wet dressings of azochloramide. The redness was therefore attributed to this. This dermatitis apparently subsided somewhat following discontinua-



Fig 14 The distention of the tumor bearing lymphatic has interfered with the nutrition of the overlying epidermis with resultant atrophy.



Fig. 9.



Fig.



Fig.

Fig. 9. Case 2, 3 months after mastectomy. The process on the opposite breast had developed into typical carcinoma erysipelatodes. Not the flaming, well demarcated border.

Fig. 10. Photograph taken with patient in same position

The lump in the upper outer quadrant of the right breast could not be palpated. A residual gland was still felt in the apex of the axilla. For sociologic reasons the patient delayed the proposed mastectomy. Aside from microcytic hypochromic anemia, her laboratory work up, as negative. The Wassermann and blood chemistries were normal.

Eleven months after admission, nontoxic nodular goiter as removed. On March, 1937, year after completion of roentgen therapy radical mastectomy as done.

**Pathology.** The specimen consisted of right breast, the underlying pectoral muscles, and axillary tissues. Extensive sectioning through the mammary parenchyma showed no gross evidence of neoplastic lesions. However the axillary tissues presented numerous discrete, firm, white, nodular areas, apparently lymph nodes, which grossly appeared to be completely replaced by neoplastic tissue. Sections through the skin showed no abnormal findings. In numerous sections throughout the breast the large ducts showed no alteration of the lining epithelium whether proliferative or neoplastic. The majority of parenchymal lobules also showed no pathological findings of note. Toward the outer upper quadrant, however, are many lobules which showed marked increase in finely dense fibrous tissue, both perilobular and periductal. Here there is considerable hyperplasia and proliferation of the lining cells of the small ducts, and in an occasional lobule some of these proliferating cells appeared distinctly atypical. The neoplastic cells are found in small sheets. They are large, with ill defined borders, pale pink or clear cytoplasm, and round nuclear nuclei with single nucleoli. A scattered perivascular lymphocytic infiltrate was found. Toward the axilla were collections of lymphoid tissue, some definitely small nodes. Several contained metastatic masses of neoplastic cells both in dilated peripheral sinuses and invading the periphery of the node. One had been completely replaced by tumor tissue. The fibrosis in the surrounding tissue as all marked here. It was fairly dense but not of the keloid type. Within the lumen of one large vessel, apparently vein, as mass of tumor cells.

The diagnosis as carcinoma of the right breast, with villary lymph node metastases. The cell type suggested duct origin. The proliferation of the duct epithelium is typical, with the fibrosis, suggested fibro-adenomatous origin. The malignancy was judged Grade 2.

After operation the patient received 300 milligram hours of radium via drains in the operant wound. Her

as in Figure 8, showing advance of lesion during 3 weeks.

Fig. Case 2, just 3 year after operation. The process had spread from the right mastectomy scar, across the anterior chest wall, and past the left axilla to the angle of the scapula.

general condition was good but persistent edema remained (the upper angle of the wound). The skin about the wound became red and tender, this improved somewhat as edema was progressed. Cultures from the chest wall and skin revealed hemolytic streptococcus, one time and staphylococcus others.

Five months after the operation, the surgeon noted that the wound was completely healed except for tiny draining sinus at the apex. The reddening of the skin surrounding this area was attributed to inflammation. Two months later this redness as interpreted as postoperative eczema. Subjective symptoms varied from slight itching to severe burning. Right supraclavicular glands were felt at this time and were treated with deep therapy. A year after the operation, the redness had spread to the posterior axillary line and was diagnosed as lymphoma. Shortly afterward, it was thought to be an eczematous lesion, possibly produced by fungus infection. Later, she was given bland ointments to apply to the reddened area. Ten years after the operation, the skin condition was thought to be due to the self application of medication. Finally however her condition was recognized as true skin metastasis. At this time, the skin presented flaming red, clearly margined, diffuse eruption which spread in all directions from the right mastectomy scar. The lesion had spread to involve the opposite breast, downward over the abdomen almost to the umbilicus, and posteriorly on to the back and shoulders, almost to the midline (Fig. 11). Biopsy of the skin showed it to be covered with thin, otherwise normal, epithelium. The rete pegs and papillary cores were all preserved. An occasional, thin, ill defined channel contained neoplastic cells with hyperchromatic angular nuclei (Figs. 3 and 4). This confirmed the clinical impression of malignant involvement of the skin.

The patient refused medical care and returned home where she died August, 1940, 13½ years following her entrance to our clinic.

Case 3. B. S. white American female aged 45 years, entered the Brooklyn Cancer Institute on May 7, 1934, complaining of a lump in the right breast of 8 months duration. Her family history as irrelevant. Eighteen years previously lactocelia, which occurred after stillbirth, as removed. Two years later after another delivery she developed multiple abscesses in the left breast, one of which was incised. Following this, the patient nursed her child on both breasts for 3 year.

siderable time elapsed between their appearance and recognition. Both were mistaken for postoperative inflammation, dermatitis venenata, fungus infection, and radiodermatitis. The medicolegal implication of the last diagnosis is significant. The diagnostic confusion could be readily obviated by prompt biopsy of any obscure lesion.

The pathological evidence would seem to indicate that the involved vessels are lymphatics. The channels containing tumor cells did not contain erythrocytes. Conversely vessels containing erythrocytes were demonstrated to be discrete from those containing tumor cells. It is conceivable that the close proximity of blood vessels to the permeated lymphatics might make them vulnerable to metastatic invasion, but we did not note this. The previously reported cases differed as to the amount of lymphatic dilatation. Serial sectioning clarified the differences by revealing the dilatation to vary between wide limits, depending upon the section examined.

Successive sections showed the lymphatics to be free from tumor cells for short distances. This raises the question of method of metastatic spread. Might this indicate that the spread was by embolization rather than permeation? This does not seem likely. The empty spaces appear to represent breaks in the advancing stalk rather than gaps between emboli. Clinically, the appearance of a well demarcated, slowly advancing and spreading lesion speaks for a steady outgrowth by permeation rather than an erratic spread by embolization. Absence of early distant metastases is indirect evidence pointing to same conclusion.

The condition appears to have sufficiently distinctive physical and pathological characteristics to warrant giving it a separate place in clinical medicine. Names implying an acute process are unfortunate. While the cases often present the startling appearance of an acute lesion, they are in fact chronic. The well demarcated, reddened, and advancing border is the only common factor with erysipelas. We would favor a pathological term implying a diffuse subepidermal carcinomatosis from carcinoma of the breast, but we believe that the addition of still another name could only add to the confusion. The term "carcinoma erysipelatodes" is sufficiently descriptive to identify the condition.

It would be of extreme importance to understand the factors responsible for making a given tumor react in a particular way, such as these two tumors have done. To venture any such explana-

tion with the information at hand would be imprudent indeed. The problem, however, should be stated for future investigation.

#### SUMMARY

1 Two typical cases of carcinoma erysipelatodes which developed in postoperative mastectomy patients are presented.

2 Both were mistaken for postoperative inflammatory complications, dermatitis venenata, fungus infection, and radiodermatitis. The medicolegal importance of this is significant. The appearance of any peculiar skin lesion following mastectomy for malignancy should be regarded with suspicion and biopsy examination made.

3 The pathological material from repeated skin biopsies was studied by serial sectioning.

4 It appears that the metastatic process, in the cases observed, is one of permeation of the subepidermal lymphatics and tissue spaces, rather than venous channels.

#### BIBLIOGRAPHY

- 1 BARBER, H. W. Paget's disease of the nipple associated with diffuse carcinomatosis of the chest wall. *Proc Roy Soc Med*, 1937, 25: 670.
- 2 DAWSON, E. K., and SHAW, J. J. M. Mammary carcinoma with generalized telangiectatic carcinoma (carcinoma erysipelatodes). *Brit J Surg*, 1937, 25: 100.
- 3 FISCHER, BRACKERTZ, MANDL, DURST, DELBANCO, CEMJACHOWSKY, and BONDARCUK. (Quoted by Pfahler and Case, loc cit, 7.)
- 4 FREEMAN, C. D., and LYNCH, F. W. Carcinoma of the breast with peculiar cutaneous metastases. *Arch Dermat & Syph*, 1937, 35: 642.
- 5 KUETTNER, H. Beiträge zur Pathologie des Mammacarcinoms. *Beitr z klin Chir*, 1924, 131: 7.
- 6 LEE, B. J., and TANNENBAUM, N. E. Inflammatory carcinoma of the breast. *Surg, Gynec & Obst*, 1924, 39: 580.
- 7 PFAHLER, G. E., and CASE, E. A. Erysipelas carcinomatous resembling radiodermatitis. *Am J Roentgenol*, 1936, 35: 804.
- 8 RASCH, C. Carcinoma erysipelatodes. *Brit J Dermat*, 1931, 43: 351.
- 9 ROTTER, H. Ueber Carcinoma Erysipelatodes. *Arch f Dermat, u Syph*, 1936, 174: 421.
- 10 RUDER, I. B. Zur Frage des erysipelas Carcinomatosis beziehungsweise subepidermalen Karzinomas der Mamma. *Zentralbl f Gynaek.*, 1928, 52: 236.
- 11 SATENSTEIN, D. L., Discussion of Freeman and Lynch, loc cit (4).
- 12 VON VONNO, N. C. A case of carcinoma telangiectaticum. *Brit J Dermat*, 1933, 45: 423.
- 13 WEBER, F. P. Bilateral thoracic zosteroid spreading marginate telangiectasis. *Brit J Dermat*, 1933, 45: 418.
- 14 Idem. Carcinoma telangiectaticum. *Internat Clin*, 1935, 3: 145.

tion of arsenic chloride and application of blood clots. Subject's symptoms consisted of moderate itching and burning. 5 months later note was made that pigmentation present on the chest all as due to radiation. Questionable small nodules were felt in the skin. It is to be noted at this time that the patient had received no post-operative radiation therapy and that any skin which might have been pigmented from pre-operative therapy had been removed at operation.

7 months later (5 months after operation) her skin condition was finally recognized as carcinoma, erythroblastosis. At this time, a semicircular scar approximately centimeters in length, as noted on the right chest wall at the site of mastectomy. From its mid point, an 8 centimeter linear scar extended transversely toward the sternum. A brownish red well demarcated discoloration of the skin, with flaming border extended medially from the lower half of the scar for distance of centimeters. The skin was slightly brown and indurated. No nodulation was demonstrable. The entire area was slightly raised (Fig. 6).

Biopsy specimens from the middle and edge of the lesion, as indicated on the photograph, revealed diffuse carcinomatous involvement of the subpapillary channels (Fig. 7). Cultures from the surface of both involved and uninvolved skin showed growth of hemolytic *Staphylococcus aureus*. The results given course of medical therapy following which there was remarkable clinical subsidence of the process. However in June, 1930, similar diffuse, red mottling was noted over the entire breast (Fig. 8). Three weeks later the appearance was typical of carcinoma erythroblastosis. The skin over the entire breast was bright red, with well demarcated, flaming edges (Figs. 9 and 10). Repeated biopsies confirmed the clinical impression. Intense deep therapy cross-firing large area, was instituted in an effort to stem the advance. Though good local response was obtained, the process continued its insidious spread. Three and half months later the flaming edge had extended posteriorly to the angle of the scapula (Fig. 11), inferiorly over the abdomen, and superiorly toward the clavicles. Roentgenograms of the chest and osseous system are negative for metastases. The right supraclavicular nodes appeared enlarged on the roentgenogram. The leucocyte count varied from 7,000 to 20,000 with 68 to 8 per cent polymorphonuclear cells.

It is remarkable that until this time constitutional symptoms were absent. Indeed, the patient felt well enough to supplement her meager income by taking in sewing. Finally in December, 1930, 26 months after her first complaint and about 6 months after skin involvement, the latter became so severe as to necessitate hospitalization. Multiple nodules and ulcerations are present over the anterior chest wall. The skin was brown and indurated with right supraclavicular and arm edema. But even at this time the periphery of the lesion resembled erythroblastosis enough to cause new surgical service to prescribe sulfanilamide. This, of course, as discontinued when the nature of the lesion was reaffirmed by biopsy.

The patient sat slowly downhill, developed jaundice, possibly due to abdominal metastases, and expired April 8, 1931, 30 months after her first complaint, and 26 months after skin involvement. Autopsy could not be obtained.

The random histologic sections of skin first studied revealed slightly dilated subpapillary channels filled with tumor cells. The uncertainty encountered in the literature as to whether they were lymphatics or capillaries still existed. In the normal skin the easily recognized subpapillary

capillary plexus and the more obscure lymphatic plexus lie in close proximity. The lymphatics are usually collapsed, resemble tissue spaces, and are nearly unrecognizable unless they contain cellular elements. When found dilated they are often mistaken for capillaries. The vascular channels in question lay so close to both these plexuses that they might have been taken for either. They were lined with single layer of endothelial cells and surrounded by a sparse infiltrate of lymphocytes. It was decided to subject the biopsy material to serial sectioning in an attempt to determine their true identity. More than 300 sections were studied.

Barring artefaction, the presence of an erythrocyte in a vessel might be taken as evidence that it was a capillary or venule. In the sections studied, no erythrocytes were found in the vessels containing tumor cells. It was assumed therefore that they were lymphatics.

In some sections the proximity of the lymphatics and capillaries were so close that the tumor masses appeared to lie in vessels containing erythrocytes. Closer scrutiny, however, always revealed the erythrocytes to be confined to capillaries which were discrete from the involved lymphatics. Occasional sections showed a capillary containing red blood cells separated from a tumor bearing lymphatic by only the single cell thickness of their respective walls. Figure 12 shows such a section where a small tumor mass appears to lie in a venule. Higher magnification reveals the tumor mass to be confined to a lymphatic which is separated from the vessel containing erythrocytes by only the single layer of cells of their respective walls (Fig. 13). In all the sections the lymphatics maintained their discrete identity in their expected anatomical location.

In some areas the proximity of the different vessels led to compression of the capillaries by distended lymphatics with resultant atrophy of the overlying epidermis (Fig. 14). Further growth of such a lesion might well lead to nodular elevation of the skin.

Serial sectioning revealed the amount of lymphatic dilatation to vary between wide limits. Single sections gave the picture at either extreme. Indeed, in an occasional section the lymphatics were so narrow as to hold only a single tumor cell. In some instances the involved lymphatics are free from tumor cells for short distances.

The metastatic process was by no means confined to the subpapillary lymphatics but involved the tissue spaces and subcutaneous fat as well.

The cases are of clinical interest because of the difficulty encountered in their diagnosis. Con-

siderable time elapsed between their appearance and recognition. Both were mistaken for postoperative inflammation, dermatitis venenata, fungus infection, and radiodermatitis. The medicolegal implication of the last diagnosis is significant. The diagnostic confusion could be readily obviated by prompt biopsy of any obscure lesion.

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Successive sections showed the lymphatics to be free from tumor cells for short distances. This raises the question of method of metastatic spread. Might this indicate that the spread was by embolization rather than permeation? This does not seem likely. The empty spaces appear to represent breaks in the advancing stalk rather than gaps between emboli. Clinically, the appearance of a well demarcated, slowly advancing and spreading lesion speaks for a steady outgrowth by permeation rather than an erratic spread by embolization. Absence of early distant metastases is indirect evidence pointing to same conclusion.

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#### BIBLIOGRAPHY

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- 2 DAWSON, E. K., and SHAW, J. J. M. Mammary carcinoma with generalized telangiectatic carcinoma (carcinoma erysipelatodes). *Brit. J. Surg.*, 1937, 25: 100.
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- 4 FREEMAN, C. D., and LYNCH, F. W. Carcinoma of the breast with peculiar cutaneous metastases. *Arch. Dermat. & Syph.*, 1937, 35: 642.
- 5 KUETTNER, H. Beiträge zur Pathologie des Mammacarcinoms. *Beitr. z. klin. Chir.*, 1924, 131: 7.
- 6 LEE, B. J., and TANNENBAUM, N. E. Inflammatory carcinoma of the breast. *Surg., Gynec. & Obst.*, 1924, 39: 580.
- 7 PFAHLER, G. L., and CASE, E. A. Erysipelas carcinomatousum resembling radiodermatitis. *Am. J. Roentgenol.*, 1936, 35: 804.
- 8 RASCH, C. Carcinoma erysipelatodes. *Brit. J. Dermat.*, 1931, 43: 351.
- 9 ROTTER, H. Ueber Carcinoma Erysipelatodes. *Arch. f. Dermat. u. Syph.*, 1936, 174: 421.
- 10 RÜDER, F. B. Zur Frage des erysipelas Carcinomatousum beziehungsweise subepidermalen Karzinomas der Mamma. *Zentralbl. f. Gynaek.*, 1928, 52: 236.
- 11 SATENSTEIN, D. L., Discussion of Freeman and Lynch, loc. cit. (4).
- 12 VON VONNO, N. C. A case of carcinoma telangiectaticum. *Brit. J. Dermat.*, 1933, 45: 423.
- 13 WEBER, F. P. Bilateral thoracic zosteroid spreading marginate telangiectasis. *Brit. J. Dermat.*, 1933, 45: 418.
- 14 Idem. Carcinoma telangiectaticum. *Internat. Clin.*, 1935, 3: 145.



## TRANSURETHRAL PROSTATECTOMY

### A Photographic Record of the Operation of Transurethral Resection

FLETCHER H. COLBY M.D. F.A.C.S. and HOWARD I. SUBY M.D. Boston, Massachusetts

**ILLUSTRATION** is an effective method of description. With advances in photographic technique pictures are taking an increasingly important place in medical writings. Operative procedures which require the use of telescopes and lens systems have fields of vision often limited to the operator alone. It is not easy for an untrained person to understand these operations, and restricted vision makes teaching difficult. Operations of this sort are more easily portrayed by illustration than description. Therefore, we have used recent improvements in photography to illustrate the operation of transurethral prostatectomy.



Fig. 1. Low spinal anesthesia. Safe, satisfactory anesthesia is obtained with 50 milligrams of novocain crystals in the fourth lumbar interspace with the patient in the sitting position.

This communication describes graphically the method employed by us for the transurethral removal of the prostate gland. The illustrations are actual photographs of the hypertrophied gland, the changes which result from obstruction, and transurethral removal of the prostate, taken with a cystoscopic camera during operation. The sharpness of the photographs is an evidence of the clear vision obtainable with modern instruments and so necessary for a successful operation.

Careful preliminary studies of patients with prostatic obstruction must be made. We feel, however, that manipulations should be as few as possible and that even catheterization is apt to be dangerous. Cystoscopic examination has led to complications so often in the past that we prefer to eliminate this procedure if possible. Cystourethrograms ( ) we believe, give a more accurate estimation of the size of the obstructing prostate and its suitability for transurethral removal than cystoscopic examination; consequently cystoscopy, with its danger and discomfort often can be eliminated. Prostates enlarged beyond a certain size obviously are best removed by open operation, preferably perineal prostatectomy. Others similarly are suited to transurethral removal. When decision is difficult cystourethrograms are helpful.

This is our usual pre-operative preparation of patients who have prostatic obstruction. General physical examination is done and includes complete blood counts, non protein nitrogen, blood sugar and Wassermann tests. Intravenous pyelograms are made; these provide a test of renal function and afford information regarding the spine and pelvis, contour of the bladder and give a fair estimate of residual urine. Patients in acute retention, those with large amounts of residual urine or with poor renal function are put on constant drainage with a Foley retention catheter. Retention catheters are immediately connected to sterile closed drainage system and irrigated as necessary with sterile boric acid solution. If the non protein nitrogen is normal, renal function adequate, the general condition of the patient good and the prostate only moderately enlarged by rectal examination, operation is considered safe without further study. Patients lik

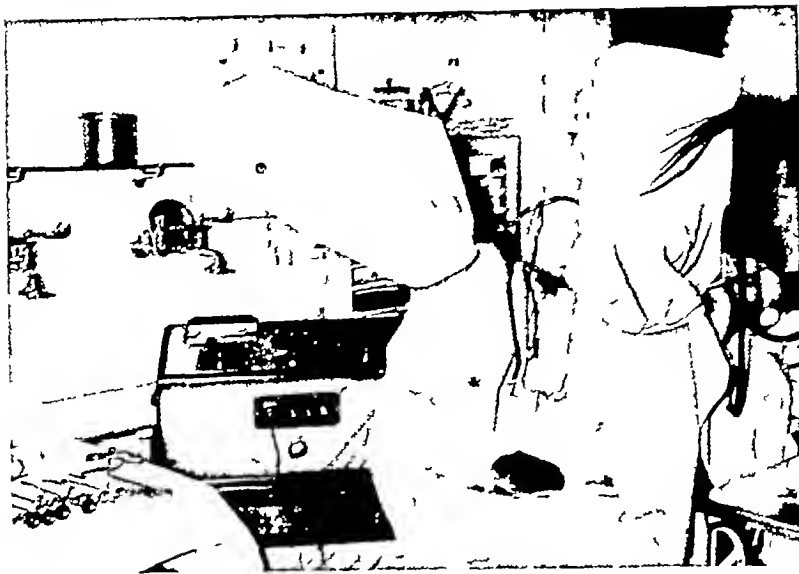


Fig 2 Preparation for operation Good exposure and complete sterility are provided Patient is in position on McDavitt-Alcock table

a history of hematuria or those with any filling defect of the bladder suggestive of tumor are examined with a cystoscope Responsibility for such complications as diabetes, cardiac disease, or others, is shared with a medical consultant We consider pre-operative chemotherapy important

Low spinal anesthesia for transurethral resection has been used by us for several years with such good results that it is now employed whenever possible This method of anesthesia amounts almost to a regional anesthetic and its level goes little higher than the symphysis pubis It has resulted in no significant falls in blood pressure and usually lasts for about one hour One hundred milligrams of novocain crystals in 2 cubic centimeters of spinal fluid is injected into the fourth lumbar interspace with the patient in the sitting position (Fig 1) The patient is kept in this position for 3 minutes after the injection This technique was described by Nesbit (2) in 1936 No complications attributable to anesthesia have resulted since its adoption

Increased comfort to the patient and better position for operating have been secured since we have used the McDavitt-Alcock table (Fig 2) Patients are as carefully prepared as for any operation and the operator wears a sterile gown and gloves

A definite routine makes for thoroughness, so examination and operation are conducted in definite sequence The bakelite sheath of the Mc-

Carthy resectoscope with Timberlake obturator is passed to the bladder and a specimen of urine is taken for culture Both the No 28 and 24 instruments are at hand since male urethras vary in size and some will not accommodate the larger sheath The bladder is carefully examined with the 90 degree observation telescope which provides a large clear field of vision The photographs demonstrate that intravesical protrusions of the enlarged prostate (Figs 6-9) and changes produced from obstruction, such as trabeculation and diverticula (Figs 3-5), are clearly discernible Further examination with the retrograde telescope, which looks toward the operator, visualizes the trigone, ureteral orifices, and internal urethral orifice (Fig 10) By replacing the retrograde telescope with the foroblique lens system, attached to the working element of the resectoscope, those portions of the prostate which encroach upon the urethral lumen are seen (Figs 11-12) The extent and variety of obstruction is thus clearly defined and operation may be started

Operation, as examination, follows a definite course The upper portions of both lateral lobes are first removed (Fig 13) These cuts are made at about eleven and one o'clock Projecting tissue at the anterior commissure is then resected Deep cuts are now made in the lower portions of the lateral lobes where they join the median lobe (Fig 14) Bleeding frequently is profuse in these areas since much of the blood supply to the lateral and median lobes is cut across A resectoscope



Fig. 2.



Fig. 4.



Fig. 5.

Fig. 2. Trabeculation. Preliminary inspection of bladder shows hypertrophied muscle bundles due to obstruction at bladder neck.

Fig. 4. Cellulitis. Another area of bladder wall shows

accumulation of mucous membrane from increased intravesical pressure.

Fig. 5. Diverticulum. A later result of prolonged obstruction is herniation of the bladder mucosa.



Fig. 6.



Fig. 7.



Fig. 8.



Fig. 9.

Fig. 6. Prostatic cyst. Clear fluid cyst on lateral lobe of enlarged prostate.

Fig. 7. Hypertrophied lateral lobe. Obstruction at bladder outlet. Diverticulum in background.

Fig. 8. Anterior commissure. Roof of prostatic urethra,

normally circular, is angulated by hypertrophied lateral lobes.

Fig. 9. Hypertrophied median lobe. Obstructing tissue bulges upward from floor of prostatic urethra. Bladder cavity shows above.



Fig. 10.



Fig. 11.



Fig. 12.

Fig. 10. Retrograde view of median lobe. Obstructing tissue of internal sphincter as it appears looking toward operator from within the bladder. Bladder base below.

Fig. 11. Mid prostatic urethra. Enlarged lateral lobes

nearly fill urethral lumen. Forbiquet telescope.

Fig. 12. Distal prostatic urethra. Vermiform appendix visible below. Lateral lobes encroach upon urethra. Loop electrode above.



Fig 13

Fig 14

Fig 15

Fig 16

Fig 13 The first cut Loop electrode has removed the first piece of tissue from upper part of right lateral lobe Bits of tissue adhere to loop

Fig 14 Deep cut in lateral lobe Repeated cuts remove the enlarged prostate layer by layer

Fig 15 Remains of median lobe A thin rim of hypertrophied prostate remains on urethral floor

Fig 16 Operation completed Obstructing tissue removed Clear view into bladder Note smooth fibrotic appearance of prostatic capsule

employs two types of current regulated by a foot switch The cutting current removes tissue, and the coagulating current is used to stop bleeding points With the bleeding of this very vascular region controlled, remaining tissue is removed with little hemorrhage Intravesical protrusions of the lateral lobes are cut away until the muscular fibers of the internal sphincter appear The striated appearance of this muscle is an important landmark which makes it plainly evident that the cuts are sufficiently deep Removal of the intravesical part of the middle lobe is simple and quickly accomplished The intra-urethral parts of the prostate are now left The lateral lobes are hollowed out layer by layer down to the verumontanum which is generally an easily seen landmark (Fig 12) Remaining tissue to be removed are the remnants of the lateral lobes and the remains of the median lobe on the floor of the urethra (Fig 15) In our experience this is removed most effectively with the Nesbit modification of the McCarthy resectoscope With a finger in the rectum remaining nodules of hyperplastic tissue are readily engaged in the loop electrode and cut away until all hypertrophied tissue is removed The rectal finger guards against cutting too deeply and avoids undue pressure of the sheath against the urethra The differentiation between normal and hypertrophied prostatic tissue is usually clear Hyperplastic tissue has a characteristic structureless frosty appearance in contrast to the gray orderly structure of the normal prostate Enlarged glands, within one's ability to resect, are thus cleanly and systematically removed (Fig 16) Cut tissue falls back into the bladder and is removed by evacuation only as is necessary for clear vision At the conclusion of the operation

bleeding points are controlled by coagulation, and a 30 cubic centimeter Foley type catheter is inserted into the bladder Tension on the bag for hemostasis is seldom necessary

Postoperative care is usually simple Catheters are connected immediately to a sterile closed drainage system and irrigated frequently enough with sterile boric acid solution to prevent clotting Sedatives and intravenous fluids are given as necessary Catheters are removed in from 3 to 5 days after operation After this the great danger of infection makes it unwise to catheterize these patients Curiosity regarding residual urine should be restrained Difficult urination or persistently cloudy urine means incomplete removal of the hypertrophied prostate and indicates the necessity of further operation The average postoperative stay in the hospital has been about 10 days

The accompanying photographs illustrate many of the steps in the transurethral removal of the prostate They demonstrate that clear and adequate vision may be obtained during operation and that those prostates suited to resection are cleanly and effectively removed by this method

#### SUMMARY

The management of the obstructing prostate and its removal by transurethral resection is described and illustrated by photographs taken at operation with a cystoscopic camera

#### REFERENCES

- 1 COLBY, T H, and SUBY, H I Cystourethrograms Roentgen visualization of the urethra, bladder, and prostate *New England J Med*, 223, 1940, 85-92
- 2 NESBIT, R M Controlled low spinal anesthesia in transurethral surgery *J Urol*, 1936, 35 557-560

# FREE BONE FLAP OSTEOPLASTIC CRANIOTOMY

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WILLIAM CONE, M.D. Montreal, Canada

THE orthodox method of osteoplastic craniotomy is to leave the bone flap attached to muscle, as was begun by Wagner 1830, 50 years ago.

In 1936 one of us (W. V. C.) commenced the use of free bone flap osteoplastic craniotomy in selected cases. The chief reason for desiring a change was that there are so many areas of the skull where muscle attachment necessitates a larger scalp and bone flap than would otherwise be required for an adequate approach to the underlying intracranial disease. Other advantages have appeared and the results have been so uniformly satisfactory that the free bone flap has been turned in an increasing percentage of operations, so that at the present time we have available over 50 cases in which the procedure was used and from which conclusions may be drawn.

The procedure is not an original one. Lenche, 1933, reports that he has completely freed the skull flap in about 30 osteoplastic craniotomies since 1919. O. Sjöqvist, in a personal communication states that he has used the method several times. Doubtless many others have employed it. This report is indicated, however, because the procedure is not yet widely recognized, because it is feared by many of those acquainted with it, and because we feel that its advantages should be brought again to the attention of those surgeons who operate on patients with intracranial disease.

## PROCEDURE

The exact localization of the lesion having been made, the scalp flap is planned in the usual manner. After hemostasis has been established along the incision line, the scalp is reflected with the raspator, the line of cleavage being between the bone and the pericranium. It is important that the pericranium be attached to the scalp, retaining its intact blood supply, because of its important rôle in bony repair. We feel that it is this osteoplastic membrane that requires nourishment—not the bone already laid down. When this scalp flap is completely turned back and all bleeding is controlled, it is wrapped in gauze moistened with Ringer's solution, is padded to prevent kinking,

and is held retracted by means of barbed fish hooks which are attached to rubber bands which in turn are attached to the adjacent drapes with Allis forceps.

Four to six burr holes are drilled at proper positions and the flap is cut out with the Gigli saw, care being taken to stagger and bevel the sawed line as described by Stookey 1937, so that the flap will interlock and be stable when replaced. Before the flap is freed, marks are made indicating the position of the punch holes for wiring the flap at the end of the operation. When the last attachment of the bone flap is being cut, extreme caution must be employed to prevent the flap being suddenly detached from the dura and dropped to the floor. When completely severed, it is dissected from the dura in the usual way (usually it lifts off with surprising ease) is wrapped in a dressing moistened with Ringer's solution, and is left on the nurse table until needed at the close of the procedure.

We have found that manipulation is avoided and time is saved if the holes for wire are introduced before the flap is laid aside in the beginning. Two or three points for wiring have proved to be sufficient. Number twenty-eight chromium steel wire is used, is tied or twisted, and the knot or twist turned into the outer hole. There is no essential change in the closure of the aponeurosis and skin.

Our patients who have had free bone flap osteoplastic craniotomies have ranged in age from 3 to 61 years. They have been equally divided as to sex. The majority have been operated on because of intracranial tumor. All areas of the convexity of the calvaria have been reflected. Because of the nature of their disease, many patients have died within a few months. However 3 patients were followed for 2 years; 1 of these patients is still living.

By way of complication, a patient developed an infection as a result of skin sensitivity to boric acid. The bone flap became involved, necessitating removal. This bone flap was a small one and was sacrificed at once without too great deformity. Had the standard larger sized attached flap been used, it too would have had to be sacrificed and a much greater deformity would

From McGill University and the Montreal Neurological Institute.



Fig 1, left Case 1 Roentgenogram showing free bone flap 6 days after operation



Fig 2 Free bone flap 5 months after operation Com-

parison of radiopacity of flap with that of the rest of skull and with appearance immediately after operation shows no absorption There is evidence of bony union

have resulted One flap was dropped on the floor during the operation It was washed with Ringer's solution, and was boiled for 10 minutes in the same solution Thus far, this has produced no demonstrable ill effect, and the flap is still satisfactory However, there has been an elapse of only 3 months

Large doses of roentgen-ray have been directed through the flap to underlying tumors on many occasions, the treatment commencing as early as the fifth postoperative day No deleterious effect has been seen following such treatment, though

there has been evidence of transitory decalcification in some instances

The results of roentgen-ray studies of these patients with free bone flap osteoplastic craniotomies likewise have been satisfactory The following brief case reports are included as objective evidence

CASE 1 E S, female, aged 10 years On August 18, 1939, a left osteoplastic craniotomy (free bone flap) was turned and a subtotal removal of a large intracranial neoplasm carried out Figure 1, is a roentgenogram showing the bone flap on August 24, 1939 She returned on January



Fig 3, left Case 2 Roentgenogram 2 days after operation showing condition of free bone flap



Fig 4 Free bone flap 11 months after operation, 5,700

r units of roentgen therapy have passed through a port centering in this region There is some evidence of central rarefaction but there is also bony union with the skull



Fig. 5, left. Case 3. Roentgenogram with flap side away from film, taken 14 days after operation.



Fig. 6, right. Case 3. Roentgenogram with flap side next to film. This ray film was taken 14 months after operation. Note the bony union and definite lack of evidence of absorption.

9, 1930 with signs of recurrence of the tumor. On that date, the roentgenogram (Fig. 5) suggests that bony union between the skull and the flap has occurred extensively. There is no evidence of absorption of bony substance in the flap.

CASE 2. M. W. female, aged 47 years. On July 7, 1933, left parietal free bone flap osteoplastic craniotomy was carried out for the relief of symptoms produced by cystic glioblastoma multiforme. On July 9, 1933, the roentgen-ray appearance was that seen in Figure 3. In the ensuing months, she received roentgen therapy totalling 8,500 milts, 5,700 of which were passed through port centering over this bone flap. In February, 1934, roentgenograms showed some resorption: i. e. the center of the bone flap but there was bony union at the edges. On June 20, 1939 there was less resorption than was found in February (Fig. 4) and bony union with the skull was more in evidence. The patient has since died. Autopsy not obtained.

CASE 3. H. McD. male, aged 6 years. On April 12, 1938, right frontal free bone flap osteoplastic craniotomy as performed and postoperative cerebrospinal cavitation drained. On April 6, 1938, roentgen ray films with the left side of the head down (Fig. 5) were taken. The patient's course has been without incident. He is our oldest patient and has one of the longest postoperative courses in our series. Figure 6 shows the appearance of the skull flap on January 6, 1940. There is bony union between the flap and the skull. There is no resorption of bone, in fact there may be some increased density.

of operative treatment of severe head injuries. In all of these situations it has been shown that the preservation and union of bone is accomplished only if the bone is freshly removed from the patient's own body and if the attachment of the periosteum to the surrounding tissues is maintained.

Boiled autopsy bone, in our experience and that of others, is absorbed within 18 months (Gurdjian, 1935). In the case of our patient whose contaminated flap was boiled, insufficient time has elapsed to enable us to submit a report on the fate of the bone. Naffziger (1935), however, has noted absorption within 8 months under similar circumstances.

The advantages to be gained by freeing the bone flap in osteoplastic craniotomy are many. Only that bone, the removal of which is necessary to visualize the intracranial lesion, has been elevated. The absence of an overhanging ledge gives greater freedom of action to all members of the operating team. The tendency for the procedure to fall into successive stages without overlap, plus the reduced flap size, facilitate speed in turning the flap and cut down blood loss. The shock almost always attending the coarse operative manipulation of cracking up the flap is avoided. Oozing of blood from the bone flap during and after operation is completely eliminated. We feel that trauma to the soft tissues is considerably less. The craniotomy can be enlarged by removing adjacent skull as an auxiliary flap, without leaving a skull defect. A decompression can be made in the usual way if desired.

It has long been obvious that bone cut free from all attachment will live if replaced in a suitable environment. We have had repeated occasion to observe the good results clinically and roentgenographically of tibial, iliac and rib grafts in the repair of old skull defects as well as elsewhere in the body. That skull bone should survive equally well has been proved in many instances in which comminuted pieces of calvaria have been temporarily removed and then replaced in the course

## SUMMARY

Free bone flap osteoplastic craniotomy is followed by wound healing that compares favorably with that observed when bone-muscle attachment is retained. Advantages to be gained are the reduced size of the scalp and bone flap usually required, reduced blood loss, reduced soft tissue trauma, increased freedom of action to all members of the operating team, increased speed in turning the flap, and elimination of the danger of hemorrhage due to blood oozing from the bone flap.

## BIBLIOGRAPHY

- 1 GURDJIAN, E. L. Management of depressed skull fractures and old skull defects. *Ann Surg*, 1935, 102: 89.
- 2 LEFRICHE, R. De l'ablation temporaire du volet osseux dans les trépanations ostéoplastiques et de sa remise en place à la fin de l'opération. *Lyon chir*, 1933, 3: 571.
- 3 NAFFZIGER, H. C. The restoration of defects in the skull. *Tr West Surg Ass*, 1935, p. 126.
- 4 STOOKLEY, B. Interlocking osteoplastic flap, method to prevent lateral movement. *Surg, Gynec & Obst*, 1937, 64: 949.
- 5 WACKNER, W. Die temporäre Resektion des Schädeldaches an Stelle der Trepanation. *Centralbl f Chir*, 1889, No. 47 p. 833.



# THE MANAGEMENT OF THE APPENDICEAL STUMP

## Inversion without Ligation of the Stump

LOUIE FELGER, M.D. F.A.C.S., Los Angeles, California

THREE basic methods are generally employed in treating the appendiceal stump. These are (1) simple ligation of the stump, (2) ligation and inversion of the appendiceal stump, and (3) inversion without ligation of the stump. Each of these procedures has its firm adherents and opponents. Each has been equally commended and condemned.

Because of the possibility of the inflammatory reaction about the stump extending to the cecum, intramural abscesses are not unlikely



Fig. 1

Fig. 1. The cecum is delivered into the wound and held by the assistant with moist sponge. The meso-appendix is then transected between clamps and ligated with plain No. 1 suture.

Fig. 2 and 3. The peritoneal cavity is well walled off with sponge and then the appendix is excised at its base between Kocher clamps. 3. The cecum is protected with gauze sponge around the clamp and the stump of the appendix is treated with phenol and alcohol.



Fig. 2



Fig. 3

Fig. 3. A Coching right angle stitch using chromic No. 1 suture on straight tapered needle is applied over the clamp. The end of this suture A is left long. The appendiceal artery not shown in this figure, is caught in this suture. 2. The clamp is then withdrawn and the suture drawn taut. Using the same suture, continuous Lambert stitch B is applied over the first suture line in the opposite direction to the first layer. 4. The suture B is then tied to the beginning of the first layer A.

The objections raised to the method of simply ligating the stump with no attempt at inversion are (1) it permits contaminated raw surface to remain free in the peritoneal cavity, (2) it violates the sound principle of serosa to serosa apposition in gastro-intestinal surgery, and (3) cases of peritonitis and fecal fistulas due to loosening of the ligature or necrosis of the stump are not infrequently reported.

There are also certain objections inherent in the method of ligation and inversion of the appendiceal stump. In this procedure an infected stump is inverted into a closed cavity—the cecal wall.

From the Department of Surgery, Cedars of Lebanon Hospital, Los Angeles, California.

We have found the ideal procedure in the management of the appendiceal stump to be inversion without ligation as opposed to simple ligation or ligation and inversion. This method is sound surgically for it approximates serosa to serosa, and inverts the crushed stump into the lumen of the cecum where drainage is adequate. It thus obviates the objections inherent in the two other methods.

In the accompanying figures together with the explanatory legends we present a method of inverting the unligated appendiceal stump. This procedure is advanced not as a new technique, but rather for the sake of emphasis. To date it has been employed successfully in well over 700 cases.

# SUPERFICIAL INFECTIONS DUE TO ANAEROBIC STREPTOCOCCI

## Indications for Zinc Peroxide Treatment

JACOB REICHER, M D, Dayton, Ohio

INITIATED by the brilliant work of Meleney and his associates, a group of uncommon, chronic ulcers has received an etiological and therapeutic elucidation which appears to have furnished medical science with a new disease and a relatively new weapon, zinc peroxide. The discoverer of this entity has given it the descriptive term "chronic, ulcerative, burrowing, non-gangrenous ulcer due to micro-aerophilic hemolytic streptococci."

Meleney emphasizes both the anaerobic and hemolytic character of the organism as well as either or both undermining and burrowing features of the ulceration. While the writer bows to Meleney's far greater experience and probably superior judgment in the description and treatment of this disease, certain features stand out in the character of 3 of 4 cases here reported as perhaps to warrant some modification in certain concepts. In 2 cases the initial infections were seen, not as ulcerations, but as a diffuse cellulitis in one and an abscess in the other. On the one hand, however, both were caused by a non-hemolytic anaerobic streptococcus, but on the other, the larger of the two assumed the character of an ulceration with burrowing and undermining features so pronounced as to warrant inclusion in this group of infections. Furthermore its response to specific zinc peroxide therapy was so spectacular as to add to the justification for its inclusion. This is described as Case 2 and is illustrated in Figures 5 to 9. The second of these 2 cases (Case 3) revealed no undermining or burrowing propensities but the only organism isolated was an anaerobic non-hemolytic streptococcus, no organism was present on the aerobic media. It is by no means typical of the group, clinically or etiologically, but is included in this report to illustrate the facts that an anaerobic streptococcus may invade without causing burrowing or undermining, and in the absence of these changes can be successfully attacked with non-oxygen-producing antiseptics. Sulfanilamide was used for a short period.

The third of this somewhat unorthodox group (Case 4) is one in which an anaerobic hemolytic

streptococcus was present in some profusion and also demonstrates that in milder cases oxygen production is not an essential requirement in the therapeutic agent. A small sinus communicating with the ulcer represented the only possible tendency to burrow. Despite the use of only mild local non-oxygen-producing antiseptics the sinus did not increase in extent. Undermining was not present. As in Case 3 sulfanilamide was used for a few days.

In his reports Meleney discusses the clinical picture and treatment of some 40 cases, 18 of which were given combined zinc peroxide and intensive sulfanilamide therapy (11). Since the publications of his descriptions eighteen cases have been added by others (1, 2, 4, 6, 7, 14, 15, 16, 17). Some of these (2 and 6), however, do not fit precisely into Meleney's criteria for the establishment of the diagnosis. The writer has had some detailed experience with 2 others, 1 of which (Case 2) as previously noted perhaps should not be included inasmuch as the causative agent was a non-hemolytic rather than a hemolytic streptococcus.

Conversely, in the 2 other infections here reported an anaerobic streptococcus was apparently either the sole or predominating invader, but with virtually complete absence of burrowing or undermining propensities in both. In one of these cases the infectious process due to a non-hemolytic organism progressed to complete healing with antiseptics simpler in character than that used for the undermining or burrowing type. Local antiseptics and, for a brief period, sulfanilamide were used effectively for the other caused by a hemolytic anaerobic streptococcus. Because these infections lacked the gross features Meleney describes they have not been included in this report as a particular variety of chronic ulceration.

The writer does not propose to offer an exhaustive summary of Meleney's laboratory, clinical, and therapeutic studies. These are, by this time, well known to all who are familiar with current literature. They are described in at least one popular textbook (5). It is one of the chief purposes of this paper to emphasize the desirability

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Fig. 1. Case 1. Illustrating the size of the lesion on the abdomen with undermining and extension onto the thigh. A probe has been inserted under the bridge of skin to illustrate communication between thigh and abdominal ulcerations. Further extension has occurred laterally between costal margin and iliac crest, with involvement of the corresponding lumbar area as illustrated in Figure 2.



Fig. 2. Case 1. A probe has been inserted into the skin and appeared to be an ulceration secondary to the primary abdominal lesion and strip of adhesive marks the site of the tip of the probe. The undermining extends laterally, as well as and communicates directly with the abdominal ulcer.

of making anaerobic cultures in all chronic superficial infections. Following this, some conditions will be offered relative to indications for the use of zinc peroxide. Parenthetically at this point mention should be made of a simple method of anaerobic culture devised by Spray and recommended by Shallow and his associates in their studies on this type of infection.

Some modifications in treatment have been suggested by various writers. Thus, while McIneny applied zinc peroxide in distilled water Pennoyer utilized hydrogen-peroxide as the suspending agent. Rhoads found that it "proved useful" to administer a zinc peroxide suspension daily as a low rectal enema in a case in which a perirectal abscess opened 4 inches proximal to the

anus. Mullen and Lawrence attempted the treatment of this infection with both sulfanilamide and



Fig. 3. Case 1. After the first few applications of zinc peroxide the granulations have assumed a gelatinous appearance. Because of the difficulty attendant upon the removal of the preparation applied the preceding day the more thinned-out portions of the undermined skin have been removed. The white flakes are remnants of the zinc peroxide suspension applied the preceding day. The crusts are noted. Figure 4 has been removed.



Fig. 4. Case 1. This area is the same as that illustrated in Figure 3 and denotes the extent to which the seemingly small ulcer has undermined. Re-examination of Figure 3 reveals normal appearance of the skin which has been undermined by the infection. Under treatment the granulations became bright pink and flush with the level of the skin and later new epithelium began to grow in from the skin borders.



Fig 5 Case 2 This photograph illustrates the extent to which the skin has been undermined as marked off by the continuous dark line. The skin overlying the liquefied subcutaneous tissue is normal in appearance, boggy, but not particularly painful or tender. The slightly darker patch like areas are due to the brownish pus which has escaped from the incisions.



Fig 6 Case 2 A "close up" view of the external appearance of the lesion.



Fig 7 Case 2 A single application of zinc peroxide has been employed but it was found impossible to remove effectively the old preparation. The area was then opened widely, revealing the foul smelling, necrotic material illustrated. The infected area was incised, not excised, and the flaps of skin have fallen away from the underlying surface. The fascia lata is exposed on the thigh.

zinc peroxide, and efforts along the same line were made in a larger series (11). Prontosil was used unsuccessfully in 1 of a series of 6 (17) although the dosage is not stated. In 1 patient Meloney used sulfanilamide alone although the clinical

course was longer than in those treated by the combined method. Goodman with equal success cured relatively small chronic, undermining ulcerations with sulfanilamide alone, as previously noted, he did not make any anaerobic studies



Fig. 8. Case . Undermining has extended so extensively into both inguinal areas, as well as the left ischioanal fossa and right buttock, that additional inguinal fascial incisions were later placed to facilitate zinc peroxide treatment. Catheters have been inserted from the open ulcerated areas of the abdomen under the skin of both groins and out through these incisions to illustrate the communication.

Ayres reported ultimate cure with maggots in ulcerations clinically resembling those described by McEneaney. Ayres spoke of the isolation of a hemolytic streptococcus but did not comment on any anaerobic studies.

The writer utilized both zinc peroxide and sulfanilamide in his 2 cases without success. However, the ulcerations were unusually extensive. In both, one patient was a diabetic and in each death occurred rather suddenly following intercurrent accidents. Both were making excellent progress and the infection was under complete control for some time before death occurred in the patients. Furthermore, oral specific medication was discontinued in the first patient because of suspected toxic reactions and not instituted until late in the second. Whatever control was effected over the disease in each should in all fairness be ascribed to the zinc peroxide alone. Cure was achieved in

the third and fourth cases with commoner antiseptics although sulfanilamide was used for a few days in each.

Some experiences with zinc peroxide acquired through efforts to cure the infections described in this report may prove useful to others. It is stated that not more than 25 grams of the zinc peroxide powder should be activated (heating at 140 degrees for 4 hours) at any one time. The writer, however, found it necessary to activate as much as 150 grams in one container and did not notice any appreciable reduction in the oxygen generating power of the preparation. A further and perhaps unimportant modification is associated with the necessity of maintaining constantly moist medium for the zinc peroxide suspension. McEneaney accomplishes this by sealing in the medication after it has been applied, by means of gauze impregnated with vaseline or zinc oxide ointment. Possibly because of the extent of the lesion in the first case or some other and terminal factor this did not prevent appreciable drying with probable resultant reduction in oxygen generation as well as increased pain on dissection and removal of the old preparation. It was therefore decided to apply fenestrated tubes on the crusts of zinc peroxide suspension with one opening of tube projecting externally from between the layers of the ointment gauze. Small quantities of distilled water were then injected at 3 to 4 hour intervals during the 24. This variation proved effective in maintaining moisture.

#### CASE REPORTS

Case (Figs. 1 to 4). A 40 year old, white man, admitted to the hospital June 27, 1938, with evidence of acute appendicitis existing for about 24 hours. He had taken saline cathartics and been examined three times with evidences of advancing peritonitis. Appendectomy with colectomy was immediately performed under spinal anes-



Fig. 9. Case 2. Should be compared with Figure 7 to illustrate the improvement after some 30 days of treatment with zinc peroxide. The granulations are bright, healthy pink color. Unlike Case 1, however, no growth of epithelioma as noted from the skin bordering the ulcer. The opening of "burr" at the anterior superior iliac spine may be noted. This continued to extend slowly along the crest of the ilium despite repeated negative anaerobic cultures and persistent use of zinc peroxide applied with narrow strips of gauze.

thetia and closed with stab wound drain. The appendix had ruptured and was found lying in a retrocecal position. Pertinent comments from the patient's progress notes follow.

On the fourth postoperative day, jaundice was noted and a doughy, virtually painless cellulitis of the right abdomen was present and extended on to the thigh and lower chest anteriorly on the right.

On the sixth day, sulfanilamide administration was started, cautiously due to jaundice. Eighty grains were given over a 2-day period, then discontinued for fear of further compromising the liver.

On the eighth day, the drain was removed. A foul smelling pus was released.

On the ninth day, patient pulled out the cecostomy tube. The sutures were removed. The wound edges gaped and the transversalis fascia was exposed.

On the eleventh day, he developed urinary and fecal incontinence.

On the twenty ninth day his general condition was some what improved, and the jaundice was subsiding. Eeecs were draining from stab wound. A slough (?) was noted within the area of cellulitis on the abdomen and thigh. Dakin's solution irrigations were instituted.

On the thirty first day improvement was noted but it was very slow in progress.

On the thirty second day azochloramide irrigation was started.

On the thirty seventh day a mixture of azochloramide peroxide was used. The icterus index was 13, blood culture, negative.

On the forty first day, anaerobic culture studies revealed the presence of an anaerobic hemolytic streptococcus. Foul pus continued to drain profusely.

On the forty fourth day a new sinus tract (burrowing area) was noted on the chest wall. The area was opened.

From the forty fifth to the seventy fifth day, there was no visible change. The ulcerating area was treated with local irrigations of urea solution, 3 per cent, and urea in hydrogen peroxide. No evidence of spread was noted.

On the eighty third day temperature was down to 100.5 degrees.

On the one hundredth day two new sinuses were noted which were filled with a foul smelling pus. Cultures here again revealed the anaerobic hemolytic streptococcus.

On the one hundred and twelfth day, zinc peroxide was started. The ulceration had assumed the appearance illustrated in Figure 1. It was not suspected that this communication with an ulcer situated in the right lumbar area (Fig. 2).

On the one hundred and thirteenth day the zinc peroxide that had been applied the preceding day was rather dry, and when it was situated under wide bridges of skin as for instance on the thigh and right flank, it was difficult to remove.

On the one hundred and fourteenth day the sinuses were excised widely. The appearance following excision is illustrated in Figures 3 and 4. Zinc peroxide was reapplied daily until grafting was done on the one hundred and forty-eighth day and moisture was maintained with fenestrated tubes.

On the one hundred and twenty third day the only organism present on aerobic and anaerobic cultures was the pyocyanus.

<sup>1</sup>During this period inquiries locally failed to elicit any information concerning the commercial availability of zinc peroxide. A letter was written to Dr. Meloney asking about the medication and he advised contacting the DuPont Chemical Company, Niagara Falls, New York. In the meantime sulfanilamide (prontylin) was again instituted and continued for a period of 7 days, then discontinued when the temperature rose to 102.4 degrees (81st day).

On the one hundred and twenty fourth day granulations were bright pink, healthy looking. The epithelium was beginning to grow into the ulcer surface from the surrounding skin.

From the one hundred and twenty fifth to the one hundred and forty seventh day local and general improvement was noted. Repeated cultures failed to reveal any organism other than the pyocyanus.

On the one hundred and forty eighth day "Seedling" grafts were peppered into the granulation on the abdomen, thigh, and back.

From the one hundred and forty ninth to the one hundred and eighty first day, successful take of most grafts was noted. By the one hundred and eighty second day there were several nummular islands of epithelium growing on the granulating surfaces. Zinc peroxide had been discontinued and normal saline dressings were used. The pyocyanus continued to grow in some profusion but repeated cultures failed to reveal any other organism. Further progress continued uneventfully until the one hundred and ninety second day when it was noted that the temperature was somewhat higher than usual (101.6 degrees). There had been a low grade elevation varying between 99 and 100 degrees throughout most of the illness. Examination failed to reveal any cause for the elevation, the granulations remained relatively clean. A careful search disclosed no new sinus tracts, the lungs were apparently clear, etc. The white cell count was 9,600 of which 73 per cent were polymorphonuclears, 22 lymphocytes, 3 monocytes, and 2 eosinophiles.

On January 6, 1939, the one hundred and ninety fifth day, the patient suddenly developed generalized clonic convulsions. Examination revealed nuchal rigidity and a positive Brudzinski sign. Non protein nitrogen was 29.5 and carbon dioxide volumes per cent was 65.6. Spinal tap revealed opaque fluid under increased pressure containing 17,000 white blood cells per cubic millimeter of which 98 per cent were polymorphonuclears. No tubercle bacilli, anaerobic or aerobic organisms were found. Mouse cultures and blood cultures were negative. Continuous spinal fluid drainage on a Bradford frame was instituted. Hourly intravenous injections of prontosil were administered.

On the one hundred and ninety sixth day patient was in a restless coma, with head pulled to the right and flaccid paralysis of the left side of the face. Breathing was stertorous. Spinal fluid was still draining. Diagnosis: Brain abscess with purulent meningitis. Temperature and pulse fell to normal levels but coma continued. At midnight, the patient expired. Consent for postmortem examination could not be obtained.

This case is typical of the infection that Meloney describes, and under zinc peroxide therapy was making excellent progress. Various other antiseptics proved worthless. Death was only indirectly due to the infection. Sulfanilamide was given at different times, then discontinued because of suspected toxic reactions, undoubtedly it had nothing to do with the favorable response shown. However, in retrospect, this patient's best chance of survival might have come with earlier recognition of the character of the lesions and perhaps immediate use of peroral sulfanilamide in conjunction with zinc peroxide locally.

CASE 2 (Figs 5 to 9) A 48 year old white man, a known diabetic, was admitted to the hospital, April, 1939, with a history of having had a urethral stricture in 1931. Eleven



days prior to admission he developed evidence of perirectal abscess. It gradually increased in size then spread over the abdomen and right thigh. Shortly after admission incisions were placed over the fluctuant areas and tubes were inserted for irrigation. The pus was foul-smelling, brown, sticky material. The overlying skin was boggy not discolored, and not particularly painful or tender. Figures 5 and 6 illustrate the lesion; the dark line delineates its extent. Aerobic culture revealed mixed infection of *Bacillus coli*, *Staphylococcus albus*, *Clostridium tetragena*, and non-hemolytic streptococcus, the latter an equally profuse growth of the non-hemolytic streptococcus on anaerobic culture. Zinc peroxide treatment was instituted but due to the difficulty encountered in removing the old peroxide the infected area was incised widely. Its appearance is illustrated in Figure 7. At this time burrowing was found to have extended into the left ischiofemoral fossa, downward on the most dependent part of the right buttock undermining the skin to the base of the penis. Additional incisions were placed to facilitate treatment of these areas. In Figure 8 catheters have been inserted to illustrate the communication between these incisions and the abdominal part of the infection. Following the institution of zinc peroxide therapy the character of the inflammation began to improve rapidly and by the twentieth day assumed the appearance illustrated in Figure 9. The granulations here are pink and healthy. However despite thorough treatment the infection continued to burrow along the right iliac crest although cultures from this area were repeatedly negative. A diffuse pitting edema of the thigh and leg made its appearance (about a month after admission). Sulfanilamide was then started, the thirty-second day after the institution of zinc peroxide treatment, and was continued for period of about weeks. Sulfanilamide blood levels during this time ranged from 3 to 10 milligrams. Burrowing continued and the use of the oral drug was stopped. (While repeated cultures showed that the infection was under complete control, at no time throughout the illness was there noted any growth of epithelioma. The patient's condition remained stationary until June 4, 1930, when he expired, 63 days after admission, of what appeared to be lung embolus. Autopsy was not obtained.)

Both burrowing and undermining features were present in Case 2 although progression was unusually rapid. This, of course may have been on account of the diabetes. On the other hand the anaerobic organism was not hemolytic and therefore this case may not dovetail precisely with McIneny's criteria. However response to zinc peroxide was excellent and the patient appeared to be making good progress only to make his exitus, like the first, as the result of an unfortunate accident. The possibility of invasion by an anaerobic streptococcus was considered immediately upon admission and zinc peroxide therapy was instituted as soon as possible after the presence of such an organism had been established. As in Case 1, early continued sulfanilamide administration might have proved more effective than the use of local treatment exclusively.

Because of the non-hemolytic character of the organism one would perhaps suspect the possible eventual development of a picture of progressive

synergistic gangrene. However burrowing propensities were too pronounced, pain relatively mild and the staphylococcus present was of the albus rather than aureus variety. McIneny has written with equal lucidity on this type of synergistic infection (3, 10).

Case 3. A 53 year old, white man, was admitted January 4, 1930, for the treatment of tender fluctuant mass measuring 4 by 6 inches and lying directly below the umbilicus. The overlying skin was not discolored. The patient stated that he had noted occasional slight discharges emanating from the depths of the umbilicus and a day prior to admission began to notice the transference for which he was admitted. Progress notes follow.

January 7, 1930. An incision, as made and the wound packed with iodoform-soaked gauze. The pus released was thick, green, foul-smelling material with an admixture of caseous particles. On culture no aerobic growth was noted, but anaerobic studies revealed non-hemolytic streptococcus.

On the sixth day after operation, improvement continued. The abscess cavity was clean and was filling in slowly. The clinical appearance was not that of burrowing or undermining type of infection.

On the eighth day after operation abscess cavity appeared to communicate with the peritoneum; the patient was having abdominal distention and good deal of pain. The white blood count was increased to 20,000. Sulfanilamide was instituted.

On the ninth day after operation pain and distention were less. Improvement continued.

On the tenth day sulfanilamide was discontinued. The blood levels of the drug for the 3-day period were 9 to 10 milligrams.

On the fifty-fourth day after operation, area was entirely healed. Patient discharged.

Case 4. A 40 year old, white man was admitted to the hospital July 9, 1931, for the treatment of chronic abscesses, abscess of the penis, acute arthritis of the left knee, and an acute infection of the left thigh. This infection of the thigh first made its appearance as an abscess which had been incised, or 3 weeks prior to admission. Healing did not follow, however and when first seen this incised abscess presented the appearance of an irregular ulcer to 5 inches in diameter and discharging rather large quantity of thick, purulent material. A small sinus was present communicating with the ulcer. Ordinary aerobic studies revealed *Staphylococcus aureus* and hemolytic streptococcus but later anaerobic cultures disclosed many long-claimed hemolytic streptococci. Sulfanilamide was instituted and after 3 days the amount of drainage had diminished considerably and after few more days, sections of iodoform-soaked—3%—and hydrogen peroxide was used locally. Oral medication was stopped the following day when it was recorded that "discharge very slight." Local antiseptics were continued until about the forty-fifth day after the beginning of sulfanilamide treatment when the ulcer had healed completely.

Except for the small persistent sinus in Case 4, which did not progress despite the use of only simple antiseptics, burrowing and undermining were absent. In other words, it would appear that the mere isolation of an organism capable of producing the disease does not warrant the clinical diagnosis unless the typical features of

undermining or burrowing is present. It is further apparent from Cases 3 and 4 that in the absence of such features one is justified in treating these patients with more conventional antiseptics. The use of sulfanilamide for a few days in each of the cases described may have played some part in bringing about a cure. It is possible, too, at least judging from Meleney's experience, that an earlier cure might have been produced if zinc peroxide had been used. However, this is relatively expensive and in the ambulant patient, apparently not necessary at least so long as no invasive tendencies are present. While cure might have been effected before the fifty-fourth day in Case 3 and the forty-fifth day in Case 4 by means of the combined treatment, it should be noted that Lawrence used zinc peroxide-sulfanilamide for a period of 3 months before he obtained cure in his case.

#### SUMMARY

Four cases are described bearing more or less definite relationships to Meleney's "chronic undermining, burrowing ulcer due to the anaerobic hemolytic streptococcus." One (Case 1) is typical in that it fits precisely in this group, the ulcer was chronic, exhibited undermining and burrowing features, was caused by the anaerobic hemolytic streptococcus, and furthermore responded dramatically to zinc peroxide treatment. In case 2 undermining and burrowing propensities were disclosed which responded equally well to zinc peroxide but was associated with a nonhemolytic anaerobic streptococcus, in other words this case may illustrate that the clinical picture can be duplicated by a different type of anaerobic streptococcus. Deaths in these patients were due to unavoidable accidents and can hardly be regarded as failures on the part of the therapeutic agent. On the contrary, the result of the use of zinc peroxide treatment in these infections was such as to lend unqualified confirmation of its effectiveness.

Cases 3 and 4 are illustrative of the fact that the significant anaerobic organism present in either Case 1 or Case 2 may be isolated in appreciable numbers from infections which do not tend to undermine or burrow. In these types cure was accomplished by simpler local antiseptics combined with short and possibly insignificant courses of sulfanilamide.

#### CONCLUSIONS

It would appear that hemolysis or non-hemolysis is not essential in producing the gross picture of the disease so long as the streptococcus is anaerobic. It is also apparent that the anaerobic

streptococcus may invade without causing undermining or burrowing. Treatment should depend on an evaluation of the combined factors of causative organism and character of the lesions. Based on the foregoing, the following corollaries may be presented:

- 1 The performance of anaerobic as well as aerobic culture studies is urged in all superficial infections, particularly if there is any tendency to chronicity.

- 2 If the infection is of recent origin, not extensive, and not characterized by undermining or burrowing, then treatment with the more conventional antiseptics should be instituted irrespective of the character of the organism isolated.

- 3 A burrowing, undermining, extensive or stubborn lesion associated with an anaerobic streptococcus, whether or not hemolytic, had best be attacked in accordance with the principles laid down by Meleney, namely, immediate application of zinc peroxide and oral sulfanilamide, 18 grains every 4 to 6 hours.

- 4 A careful watch should be maintained throughout the course of the ulceration for the appearance of any new undermining or burrowing areas.

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#### REFERENCES

- 1 ANDREWS, C. R. Chronic undermining ulcers. *J Med Ass Georgia*, 1938, 27: 446-448.
- 2 AYRES, SAMUEL, ANDERSON, H. P., and TAYLOR, G. M. Maggot therapy in dermatologic practice. *Arch Dermat Syph*, 1936, 33: 21.
- 3 BREWER, G. S., and MELENEY, F. L. *Ann Surg*, 1926, 84: 438.
- 4 Case Report, Massachusetts General Hospital. *N England J Med*, 1936, 215: 629-632.
- 5 CHRISTOPHER, FREDERICK A. *Textbook of Surgery*, 2d ed., p. 109. Philadelphia: W. B. Saunders Co., 1939.
- 6 GOODMAN, M. H. Chronic streptococcic ulcer of the skin, unresponsive to local therapy but cured by sulfanilamide, report of two cases. *J Am M Ass*, 1938, 111: 1427-1431.
- 7 LAWRENCE, K. B. Sulfanilamide therapy in chronic, undermining streptococcal ulcer. *N England J Med*, 1940, 222: 573.
- 8 MELENEY, F. L. Zinc peroxide in treatment of microaerophilic and anaerobic infections. *Ann Surg*, 1935, 101: 997-1011.
- 9 Idem. Zinc peroxide in surgical infections. *Surg Clin N America*, 1936, 16: 691-711.
- 10 Idem. *Ann Surg*, 1931, 94: 961.
- 11 MELENEY, F. L., and HARVEY, H. D. Combined use of zinc peroxide and sulfanilamide in the treatment of chronic, undermining, burrowing ulcers due to the micro-aerophilic hemolytic streptococcus. *Ann Surg*, 1939, 110: 1067-1094.

- MELONEY F L and JONES B A Prophylactic and active treatment of surgical infections with zinc peroxide. *Surg Gynec. & Obst.* 937 64 387-392.
2. Idem. Experiences in the treatment of chronic, undermining, burrowing ulcers with zinc peroxide. *Surgery* 937 69-
14. MILLER, BERNARD P Chronic, undermining, burrowing ulcer of the abdominal wall. *Northwest Med.* 937 30 32-34.
5. PERDNER, G A J Value of zinc peroxide in the treatment of chronic undermining, burrowing ulcer due to the micro-aerophilic hemolytic streptococcus. *Ann. Surg.*, 937 66 143-145.
6. RICHARDS, J E Use of zinc peroxide in the treatment of micro-aerophilic infections. *Surgery* 937 937
7. SHALLOW THOMAS A FRY KENNETH E and POLASKI, EDWIN J The effect of zinc peroxide treatment on ulcers due to the micro-aerophilic hemolytic streptococcus. *Surg. Gynec. & Obst.*, 940, 70 987-995.
8. SUGA R. S An improved anaerobic culture dish. *J. Lab. & Clin. Med.* 930, 16 203-206

# VARUS DEFORMITY OF ANKLE FOLLOWING INJURY TO DISTAL EPIPHYSEAL CARTILAGE OF TIBIA IN GROWING CHILDREN

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THE development of a varus deformity of the ankle following injury to the distal epiphysis of the tibia in growing children is uncommon. Nevertheless this condition is of great interest to the surgeon because its correction is often attended by many difficulties. In this article it is our object (1) to show that the deformity follows a specific injury of the medial malleolus, (2) to emphasize that the surgeon, may, by this knowledge, prevent the occurrence and progression of the deformity by relatively simple procedures, (3) to present fundamental principles of treatment which have given excellent anatomical and functional restoration in a neglected case with severe deformity.

## ANATOMY OF THE EPIPHYSEAL CARTILAGE PLATE AND THE EPIPHYSIS

In fetal life the future long bone is composed of a cartilaginous rod. The central portion of this rod, the diaphysis, is invaded by blood vessels and ossification progresses from this central region toward each end. The cartilaginous ends of this rod, known as the epiphyses, are invaded at a later date by separate blood vessels, and their centers become ossified. The periphery of the epiphysis remains cartilaginous, the distal rim becoming the articular cartilage, and the proximal portion remaining as a band of actively proliferating cartilage cells. This band or plate is known as the epiphyseal cartilage plate. Longitudinal growth occurs by a process of degeneration and calcification in the columns of cartilaginous cells which are invaded by bone forming elements from the diaphysis. Anatomically and developmentally this cartilage plate is an integral part of the epiphysis, and as such receives its blood supply from the same vessels.

## RELATION OF AGE TO THE TYPE OF EPIPHYSEAL INJURY

In infancy and early childhood, the connection between the epiphyseal cartilage plate and the

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diaphysis is very loose, and, on purely anatomical grounds it would be expected that shearing forces would most likely result in separation in the zone of calcifying cartilage without involvement of the cartilage plate. Haas showed that this is actually the case in young puppies and furthermore that disturbance of growth does not follow. It is of common clinical experience that, in children from birth to 9 years of age, pure epiphyseal separation as a result of indirect trauma is the rule, and deformity or disturbed growth almost never occurs. In this age group, crushing injuries alone damage the epiphyseal cartilage and give rise to disturbance of growth.

In older children, from 9 to 14 years of age, union between the epiphysis and diaphysis is more firm. This results from the fact that the band of cartilage cells becomes narrower and the line between the epiphysis and diaphysis presents an interlocking parallel surface. Consequently, in this age group, pure epiphyseal separation is rare and two main types of injury are most common.

In the first type, the line of separation may pass through the metaphyseal region up to a point where union between the epiphysis and diaphysis is very firm and the diaphysis itself becomes a relatively weaker structure than the epiphyseal cartilage. Therefore, the line of separation crosses the diaphysis, resulting in fracture. This may be properly called a fracture-separation. In this type of injury the epiphysis and the epiphyseal cartilage plate, although widely displaced are left intact. In such instances there is no direct injury to the cartilage cells and disturbed growth does not follow.

In the second type of injury, the epiphysis itself may be fractured as a result of a combination of the anatomical configuration of the region involved and the specific mechanism or direction of the force. The line of fracture may pass through the epiphysis, across the cartilage plate, and then may either proceed through the metaphysis or through the adjoining diaphysis. Only in this type of indirect injury would disturbances in growth be expected to follow. It will be shown that, due to the anatomical configuration of the

- MELICKY F L and JOHNSON B A Prophylactic and active treatment of surgical infections with zinc peroxide. *Surg. Gynec. & Obst.* 937 64 387-392.
3. Iden. Experiences in the treatment of chronic, underriding, burrowing ulcers with zinc peroxide. *Surgery* 937 69- 2.
  4. MULLIKY BERNARD P Chronic, underriding, burrowing ulcer of the abdominal wall. *Northwest Med.* 937 36 32-334.
  5. PENNABYER, G W P Value of zinc peroxide in the treatment of chronic, underriding, burrowing ulcer due to the micro-aerophilic hemolytic streptococcus. *Ann. Surg.*, 937 66 243-245.
  6. RHOADS, J E Use of zinc peroxide in the treatment of micro-aerophilic infections. *Surgery* 1937, 937
  7. SHALLOW THOMAS A FRY KENNETH E, and PULASKI, EDWIN J The effect of zinc peroxide treatment on ulcers due to the micro-aerophilic hemolytic streptococcus. *Surg. Gynec. & Obst.*, 940, 70 987-994.
  8. SMITH R. S. An improved anaerobic culture dish. *J. Lab. & Clin. Med.* 930, 6 303-306.

legs depending upon the age of the patient and his individual potentialities of growth

A variation in the deformity may be produced if the internal malleolus is displaced far medially (Fig 1 c). Thus Compere, 1935, reported an unusual case in a boy 14 years of age who had suffered a fracture 2 years previously at the age of 12. In this instance the bony configuration was atypical in that the medial malleolus was absent from its usual position at the ankle mortise but was fused to the shaft of the tibia at the level of a line of arrested growth about 15 centimeters above the growing cartilage plate (Fig 1 d). The articular surface of the tibia was not tilted and the cartilage plate, although not so wide as usual, was horizontal and growing. An identical case was reported by Van Assen in a girl 13 years of age who had had a fracture at the age of 10 years. In these two instances the medial malleolus must have been displaced rather far medially and slightly upward so that, when healing was complete, the malleolus had united with the shaft, but, because of insufficient contact, had failed to unite with the undamaged lateral portion of the epiphysis. After a temporary period of retardation of growth, as evidenced by the line of arrested growth, linear growth continued in almost a normal manner, leaving the malleolus fused to the shaft of the tibia to mark the level at which the injury occurred. No tilting of the articular surface of the tibia resulted because the medial malleolus did not lock the undamaged lateral portion of the epiphyseal plate to the diaphysis, as happens in most instances. A varus deformity resulted, not from a tilt of the articular surface of the tibia, as in most of these cases, but from a medial shift of the astragalus and foot due to loss of the normal medial support of the internal malleolus which was absent from its normal position.

Many other instances of disturbance of growth at the ankle have been reported following severe crushing injuries, operative procedures and infection which have given rise to various deformities but do not cause such typical and definite bony changes as results from adduction injuries.

#### LITERATURE

Poland, 1898, reported his case and reviewed those previously recorded by Bouchut, 1867, Rose, 1882, Hutchinson, 1885, Davies Colley, 1888, Owen, 1891, and Moullin, 1892. More recently, Smith, 1921, Baldrian, 1933, Van Assen, 1933, Brockman, 1934, Aitken, 1936, Morris and Downing, 1936, and Burrows, 1937, reported similar instances. A study of these reported cases con-

firms the fact that in most instances, the deformity follows an adduction force which results in fracture of the medial malleolus.

Correction of the deformity by osteotomy of the tibia and fibula during the growing period was found to be unsuccessful because continued growth from the undamaged lateral portion of the epiphysis of the tibia and from the fibula caused recurrence of the deformity. Ollier, however, in treating a similar deformity, successfully equalized the lengths of the tibia and fibula by chondrectomy of both epiphyses of the fibula. It is of especial interest that, as early as 1873, he performed epiphyseal fusion as a means of limiting longitudinal growth in the correction of deformity of the lower extremities. Poland, and later Brockman and Burrows, performed osteotomy of the tibia and fibula in conjunction with excision of the epiphyseal cartilage of the lower fibula, and obtained permanent correction of the deformity in growing children. McFarland, Brockman, and Burrows utilized the open wedge osteotomy of the tibia to increase the length of the leg in young children. Morris and Downing waited until growth was completed and then performed an ingenious high step osteotomy of the tibia so designed as to allow rotation and sliding of the fragments in apposition. The leg was held by a device for lengthening the tibia which allowed slow correction of deformity and lengthening.

The following case illustrates the problems presented, and the methods of their solution in the correction of this severe deformity, and the equalization of the length of the legs.

#### CASE REPORT

C.P., a boy 15 years of age, entered the hospital on December 1, 1938. At the age of 10 years he had been struck by an automobile and his right ankle had swelled very badly. The boy's mother said that x-ray examinations made at the time of injury showed no fracture at the ankle. We were unable to obtain the films as no record of them was kept by the physician in charge of the case at that time. The foot had been encased in a plaster cast for 6 weeks and then normal activity had been resumed. Nothing abnormal was noted until 2 years after the accident when the mother observed that the right foot was offset inward and the lateral malleolus was prominent. This deformity increased to a marked degree but the boy was able to continue normal activity. He had no pain in the ankle, knee, or foot but, by reason of the inversion and shortening, he developed a limp.

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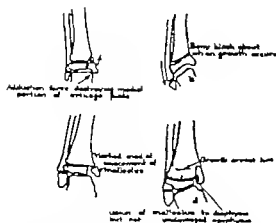


FIG. a, b, The mechanism of production of the typical varus deformity. c, d, The mechanism of production of the typical deformity (Comper and Van Assen's)

ankle, this type of fracture results most commonly from only one type of indirect violence

#### RELATION OF THE MECHANISM OF INJURY TO THE TYPE OF FRACTURE SEPARATION OF THE DISTAL EPIPHYSIS OF THE TIBIA IN GROWING CHILDREN

Bishop, 1932 made a detailed study of 32 cases of fracture-separation of the distal epiphysis of the tibia in children and found a frequency of 1 to 10 as compared to fractures of the ankle in adults. When these were classified according to the mechanism of production in the manner in which Ashhurst classified fractures of the ankle in adults, it was shown that abduction, external rotation, and torsion produced pure separation in young children but, in older children these injuries produced separation of the intact epiphysis with associated diaphyseal fracture. No fracture of the epiphysis or the epiphyseal cartilage plate resulted.

Adduction injuries, however were by far the most common, comprising 54.8 per cent of Bishop's entire series. In younger children pure epiphyseal separation occurred, but in the older group most injuries of this type resulted in a strikingly uniform vertical line of fracture running from the surface of the joint adjacent to the internal malleolus, up to the epiphyseal plate, through it, and either inward to its medial aspect or upward a short distance through the diaphysis.

Only in these cases of indirect injury is the continuity of the epiphyseal cartilage broken, and only in these is deformity to be expected. Bishop saw no instances of delayed growth or deformity

in his series but admitted that the follow-up was insufficient.

McFarland, 1932 reported that in 2 years he encountered in his English practice 23 cases of this particular epiphyseal fracture in a total series of 3,000 fractures 40 per cent of these patients developed deformity. This injury resulted most often from a fall with the feet wedged between the railings of a picket fence, and McFarland attributed the high incidence of the deformity in England, as compared to that in the United States, to the relative prevalence of picket fences in England.

#### THE MECHANISM OF PRODUCTION OF THE VARUS DEFORMITY FOLLOWING FRACTURE-SEPARATION OF THE MEDIAL MALLEOLUS

As McFarland pointed out, the anatomical configuration of the ankle makes injury in adduction the mechanism whereby premature cessation of growth occurs on the medial aspect of the epiphyseal cartilage plate. The astragalus is firmly held by the internal and external malleoli. Therefore lateral motion is not free, and an adducting force drives the astragalus against the rigid internal malleolus resulting in a localized fracture across it at this point. The malleolus is separated, the periosteum is torn and its attached cartilage plate suffers some loss of blood supply (Fig. 1 a). Degeneration of the cartilage follows and bony fusion occurs between the diaphysis of the tibia, the internal malleolus and the lateral portion of the epiphysis, forming a small rigid point about which the intact and undamaged lateral portion of the cartilage plate grows. The distal epiphysis of the fibula, not being involved, continues to grow and curves around the lateral aspect of the tibia forming a definite prominence in that region (Fig. 1 b). The typical varus deformity is formed in this manner. In some instances, however the fracture may be a mere crack with so little damage to the cartilage plate or its blood supply that no disturbance results. In others, the patient is of an age at which cessation of growth is so near that no deformity can be produced.

At first, because of the cessation of growth on the medial portion of the cartilage plate shortening is present only on the medial side of the ankle. Later there is usually found increasing shortness of the entire tibia as compared with that on the uninjured side. This follows because in most instances, when one portion of a cartilage plate is destroyed, the undamaged portion grows at a slower rate and fuses prematurely. Continued growth of the normal tibia gives rise to various inequalities of the comparative length of the two

legs depending upon the age of the patient and his individual potentialities of growth.

A variation in the deformity may be produced if the internal malleolus is displaced far medially (Fig 1 c). Thus Compere, 1935, reported an unusual case in a boy 14 years of age who had suffered a fracture 2 years previously at the age of 12. In this instance the bony configuration was atypical in that the medial malleolus was absent from its usual position at the ankle mortise but was fused to the shaft of the tibia at the level of a line of arrested growth about 15 centimeters above the growing cartilage plate (Fig 1 d). The articular surface of the tibia was not tilted and the cartilage plate, although not so wide as usual, was horizontal and growing. An identical case was reported by Van Assen in a girl 13 years of age who had had a fracture at the age of 10 years. In these two instances the medial malleolus must have been displaced rather far medially and slightly upward so that, when healing was complete, the malleolus had united with the shaft, but, because of insufficient contact, had failed to unite with the undamaged lateral portion of the epiphysis. After a temporary period of retardation of growth, as evidenced by the line of arrested growth, linear growth continued in almost a normal manner, leaving the malleolus fused to the shaft of the tibia to mark the level at which the injury occurred. No tilting of the articular surface of the tibia resulted because the medial malleolus did not lock the undamaged lateral portion of the epiphyseal plate to the diaphysis, as happens in most instances. A varus deformity resulted, not from a tilt of the articular surface of the tibia, as in most of these cases, but from a medial shift of the astragalus and foot due to loss of the normal medial support of the internal malleolus which was absent from its normal position.

Many other instances of disturbance of growth at the ankle have been reported following severe crushing injuries, operative procedures and infection which have given rise to various deformities but do not cause such typical and definite bony changes as results from adduction injuries.

#### LITERATURE

Poland, 1898, reported his case and reviewed those previously recorded by Bouchut, 1867, Rose, 1882, Hutchinson, 1885, Davies Colley, 1888, Owen, 1891, and Moulin, 1892. More recently, Smith, 1921, Baldrian, 1933, Van Assen, 1933, Brockman, 1934, Aitken, 1936, Morris and Downing, 1936, and Burrows, 1937, reported similar instances. A study of these reported cases con-

firms the fact that in most instances, the deformity follows an adduction force which results in fracture of the medial malleolus.

Correction of the deformity by osteotomy of the tibia and fibula during the growing period was found to be unsuccessful because continued growth from the undamaged lateral portion of the epiphysis of the tibia and from the fibula caused recurrence of the deformity. Oller, however, in treating a similar deformity, successfully equalized the lengths of the tibia and fibula by chondrectomy of both epiphyses of the fibula. It is of especial interest that, as early as 1873, he performed epiphyseal fusion as a means of limiting longitudinal growth in the correction of deformity of the lower extremities. Poland, and later Brockman and Burrows, performed osteotomy of the tibia and fibula in conjunction with excision of the epiphyseal cartilage of the lower fibula, and obtained permanent correction of the deformity in growing children. McFarland, Brockman, and Burrows utilized the open wedge osteotomy of the tibia to increase the length of the leg in young children. Morris and Downing waited until growth was completed and then performed an ingenious high step-osteotomy of the tibia so designed as to allow rotation and sliding of the fragments in apposition. The leg was held by a device for lengthening the tibia which allowed slow correction of deformity and lengthening.

The following case illustrates the problems presented, and the methods of their solution in the correction of this severe deformity, and the equalization of the length of the legs.

#### CASE REPORT

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His family and past history was negative. His health was good, and physical examination was negative except for the right ankle, which was seen to be in marked varus. The external malleolus was very prominent and appeared to curve around the distal portion of the tibia (Fig 2a). The internal malleolus was very small. Motions at the ankle were: dorsiflexion, right 10, left 15 degrees, plantar flexion, right 45, left 45 degrees, inversion, right 30 to 45, left 45 degrees, eversion, right -40 to -30, left 0 to 10 degrees.



Teleroentgenograms showed that the articular surface of the tibia was tilted medially 30 degrees (Fig. 3). By measurement, the lengths of the right and left tibia were 14 1/2 inches, tip to tip—straight line—right, 13 1/2 left, 13 1/2 inches; tibia, medial edge of superior articular surface to tip of medial malleolus, right, 13 1/2 left, 13 1/2 inches; lateral edge of superior articular surface to lateral tip of inferior articular surface, right, 13 1/2 left, 13 1/2 inches.

Realizing the difficulties encountered by previous surgeons, it was decided to plan the operation in detail by means of x ray films and dissections on the cadaver. The site and type of osteotomy were decided upon by tracing the teleroentgenograms of the deformed side and the normal side and by trial and error it was found that a very low oblique osteotomy of the tibia, passing laterally and distally would, if opened on the medial side, give added length, full correction, and a normal contour to the ankle (Fig. 4).

In order to safeguard the procedure a modification of a tibial lengthening apparatus was devised. It consisted of two parallel longitudinal threaded bars held at each end by curved metal pieces which were adjustable as to width. Pin carriers were mounted on the bars. These were constructed so as to hold each pin securely and allow it to be raised or lowered separately. Threaded stainless steel pins were to be used as they would allow no lateral sliding of the bones on the pin. Traction was to be obtained by the use of steel springs which would slide on the parallel bars and would be tightened by nuts threaded on the bars.

When the apparatus was tested on the cadaver it was found that, when the lower fragment of the tibia was rotated downward and around, the heel cord, the extensors and flexors of the toes, and the tibialis anticus and posticus tendons became tight and prevented rotation of the distal fragment of the tibia. It was therefore decided that these tendons should be lengthened. It was also noticed that the lower fragment of the fibula must move independently of the upper fragments of the tibia and fibula. As the interosseous membrane would tend to limit this motion, it was decided to separate this membrane from the bones about 1 inch above and below the sites of osteotomy of the tibia and fibula.

The operation was performed on December 8, 1938. Three incisions were used, the anteromedial portion of the ankle being spared because of the possibility of slough.

The first, or anterolateral, incision was begun about 1 1/2 inches above the ankle joint and was carried vertically downward for about 10 inches, being placed approximately over the course of the tendon of the extensor hallucis muscle. The tendons of the tibialis anticus, extensor hallucis, and extensor digitorum communis were exposed, and each was lengthened by simple Z method and sutured with silk. This wound was then closed.

The second incision, as made on the posteromedial aspect of the ankle, beginning at the level of the medial malleolus, and was carried vertically upward for a distance of 5 inches. The tendons of the tibialis posticus and flexor digitorum communis were immediately isolated. The posterior tibial vessels and nerves are isolated, dissected free, and carefully retracted. The Achilles tendon was exposed and lengthened about 1 1/2 inch by the method of Hoke. The posteromedial aspect of the tibia was exposed by retracting the neurovascular bundle laterally and the flexor digitorum communis tendon medially.

The third, or posterolateral, incision was begun just posterior to the tip of the fibula and was carried upward for a distance of 1 1/2 inches. The distal fibula was exposed and, with sharp chisel, very thin slices of bone was removed from the surface of the fibula to expose the epiphyseal cartilage which was then excised.

The interosseous membrane was exposed and cut for a distance of 1 1/2 inches to free the distal portion of the fibula from the tibia. The separation was continued downward thus partially dividing the syndesmosis at the tibiotalar joint. In this region many branches of the peroneal artery were cut and tied. With the peritoneal elevator the lowermost fibers of origin of the flexor hallucis longus were separated from the medial surface of the fibula. With the Mayo saw, an oblique osteotomy of the fibula, passing distally and laterally, as performed about 1/2 inch above the epiphyseal line. A Bennett retractor was placed through the interosseous membrane around the anterolateral aspect of the tibia to protect the anterior tibial vessels and nerves. With the posterior surface of the tibia then exposed, drill hole was placed through the posterior cortex of the tibia about 1 inch proximal to the site of the osteotomy of the fibula. With the Mayo saw the lateral half of the tibia was cut at an angle of 45 degrees with the shaft of the tibia.

In similar manner, but through the posteromedial incision, the medial half of the tibia was divided in the same line.

A Matthew's wire was placed through the tibia in the region of the tibial tubercle, 1 right earlier to the skin and second one placed only through the medial side of the tibia about 1 1/2 inches below and parallel to the first. These pins and the Matthew's stirrup are incorporated in the lengthening apparatus and correction as begun. Medial correction was immediately obtained, the osteotomy opening about 1/2 inch on the medial side. The tendon of the tibialis posticus muscle became tight and was lengthened by simple Z method. Flakes of osseous bone were obtained from the posterior flange of the femur and were packed into the open wedge in the tibia. The wounds were closed and the patient was placed in bed with the leg suspended in Thomas splint. His peroneal attachment and the attached apparatus as suspended separately with weights (Figs. 5 and 6). Unfortunately the apparatus was not counterbalanced sufficiently and in 10 days an area of pressure necrosis appeared on the heel. This was later covered by skin graft with excellent results.

Circulation was excellent at all times and 8 days after operation lengthening was begun again. On December 20, some flexion of the terminal phalanx of the great toe was noted. This, no doubt, was caused by the lengthening of the extensor hallucis without lengthening of the flexor hallucis. This was not distressing, however and was easily corrected by traction with small elastic bands.

Lengthening was continued slowly. Tibial pins met January 4, 1939. Less fall correction had been obtained. At this time tendency toward calcaneus was noted. On February almost 2 months after operation, traction was released. Two days later amputated cast was applied while the foot was still in the apparatus and the pins were

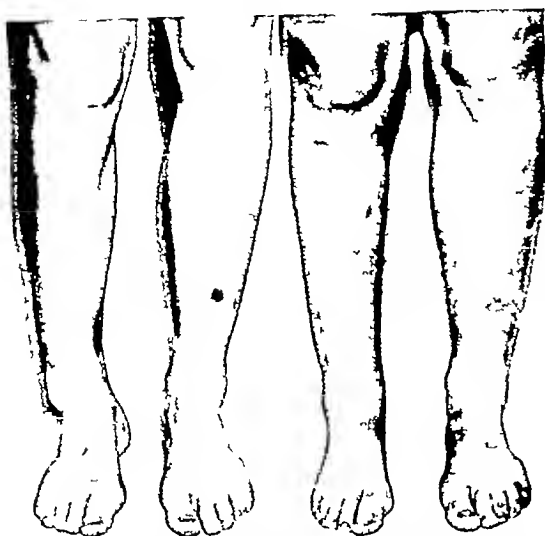


Fig 2 a, left, Photograph showing marked varus deformity 5 years after original injury b, Photograph taken on January 23, 1940, 13½ months after operation, showing the end result

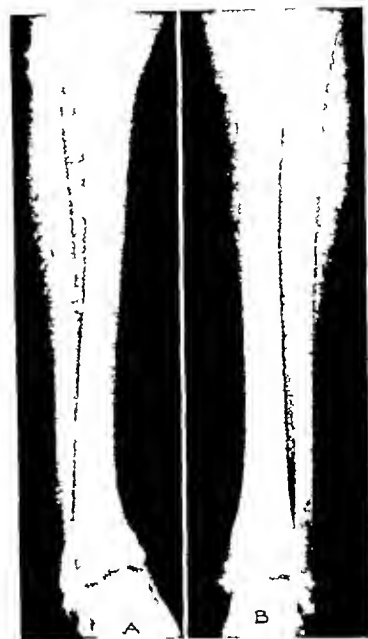


Fig 3 a, Right tibia b, Left tibia The lower articular surface of the right tibia is tilted 30 degrees Note the overgrowth and curvature of the external malleolus

removed when the cast had hardened. Clinically the osteotomy seemed to be solid. A walking iron was applied and the patient walked in this until March 30, when it was removed and he walked without support. There was no pain in the ankle but he still had a slight lump due to the shortening which remained. Some edema occurred, but this gradually disappeared.

On April 6, 1939, teleroentgenograms of the tibia showed the following measurements: fibula, tip to tip—straight line—right 15¼, left 15¾ inches, tibia, medial articular ledge to internal malleolus, right 15, left 16 inches.

The medial side of the right tibia had been lengthened ¾ inch and the left tibia had grown slightly during the time of observation (Fig 7).

Because it was thought that the difference of 1 inch in length would probably increase to about 1¼ to 1½ inches at completion of growth, it was decided to close the upper epiphyses of the tibia and fibula of the normal left leg. We estimated that, by performing such a procedure, the difference of 1 inch might be decreased to ¾ or ½ inch through growth in the proximal epiphysis of the right tibia. Accordingly this operation was performed on June 17, 1939, and at the same time the right foot was gently manipulated to increase the motion at the ankle.

This patient was discharged from the hospital on July 2, 1939, walking very well with excellent power in all muscles. Motions of the right ankle were as follows: dorsiflexion, 10 degrees, plantar flexion, 30 degrees, eversion, 10 degrees, inversion, 10 degrees.

He was last seen on February 2, 1940, 14 months after operation. At that time the correction had been maintained and he had full use of his foot and ankle, even indulging in such strenuous sports as basketball and football without pain (Fig 2b). Teleroentgenograms showed that the inequality in length had not changed although the upper epiphysis of the right tibia was still unfused (Fig 8). It is probable that the expected decrease in the inequality will not be obtained as the skeletal maturation of this boy is rather far advanced.

#### TREATMENT IN EARLY AND ADVANCED CASES

The surgeon treating fresh fractures through the medial portion of the distal epiphysis of the tibia should insist upon careful radiological check-up every 6 months until it is certain that no disturbance of growth is developing. The earliest sign of impending difficulty is an area of fusion between the medial malleolus and the diaphysis.

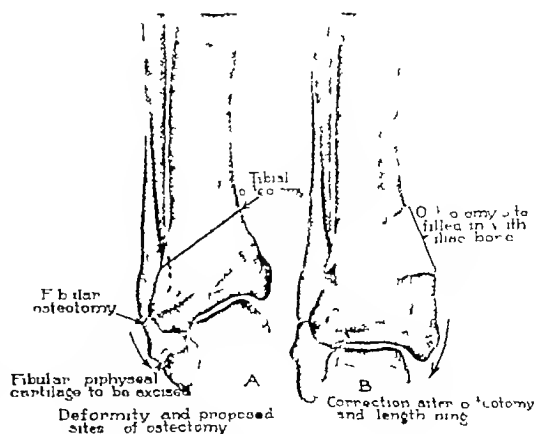


Fig 4. Proposed plan of operative correction. Compare with Figure 7 to see how closely this was achieved

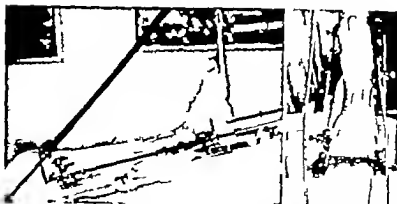


Fig. 5 Tibia incorporated in lengthening apparatus and suspended in Thomas splint after operation

with the disappearance of the clear area occupied by the epiphyseal cartilage plate. If it becomes obvious that varus deformity is developing and the child is of an age which the amount of growth to be expected would cause considerable deformity, simple fusion of the lateral growing portion of the distal epiphysis of the tibia and the distal epiphysis of the fibula of the affected leg would result in clinical cure as the other joints of the foot could easily compensate for the minor tilt already present. Attendant fusion of the distal epiphyses of the tibia and fibula of the normal leg would then assure practical equality in the length of the legs at full growth. In this manner relatively simple procedures would save the patient not only from the discomfort of the developing deformity but from a major operative procedure in the future.

The objection might then be raised that this procedure would give rise to too great a decrease in total height. From the age of 9 or 10 years, however, the growth from the distal epiphysis of the tibia amounts to no more than 2 inches in most cases, so that this loss would be of no great consequence if the legs maintained equal length. In older children the loss in height would be even less.

For the patients who have considerable deformity when first seen, but who are still growing, Poland, Balkman, Van Assen and McFarland advocated delay in the correction of deformity until near the time for cessation of growth, unless disturbances in the knee or foot cause pain or discomfort. In the light of our present knowledge this course does not seem justifiable.

During the production of this deformity small compensatory changes develop in the joints above and below it, so that when the main deformity

itself is fully established compensatory changes in the small joints of the foot are already present. This was clearly shown in our case when it was found that had the articular surface of the tibia been brought to an angle of 90 degrees with the line of the shaft, the foot would have been carried into a position of very evident valgus.

For this reason it seems much more reasonable to correct the deformity immediately and Eile Brockman, to close the distal epiphysis of the fibula and the growing lateral portion of the epiphysis of the tibia. In order to insure that the two legs will be of nearly equal length at full growth, the correction should be accompanied by closure of the distal epiphyses of the tibia and fibula of the normal leg. To equalize discrepancy in length of the tibias already present, closure of the upper epiphyses of the tibia and fibula of the sound leg could be performed at the proper time as determined by known rates of growth.

In the cases in which deformity is already advanced, correction should be planned to give as much increase in length and anatomically perfect a result as possible. Added length is obtained by an osteotomy wedged open on the medial side. A low oblique osteotomy planned so that it passes through the region of the deformity will give added length and a good anatomical and cosmetic result, and will not merely insert another deformity in the opposite direction as does the usual higher osteotomy. In the growing child the low oblique osteotomy will also accomplish closure of the growing lateral portion of the cartilage plate as it passes into the cartilage on the lateral side. This osteotomy passes through a region of the tibia too where union is sure and rapid.

Cancellous bone from the ilium, in the form of thin slices or flakes, is suggested as an advantage



Fig 6 Roentgenograms taken 13 days after operation. The tilt of the articular surface of the tibia is almost fully corrected. Notice the iliac bone packed into the osteotomy site in the tibia.



Fig 7 Roentgenograms taken 4 months after operation. Complete union present.

geous and easily obtainable material to fill in the wedge. Because of its plasticity, it packs into position easily and adjusts to the increasing size of the wedge during the slow postoperative correction of the deformity. One of us (LCA) has used cancellous bone from the ilium in a great diversity of conditions for many years. Its relatively early revascularization and reossification when compared to that of cortical bone has always been impressive. When used in filling bony defects where strength and rigidity are necessary, wedges of the desired shape may be cut from the full thickness of the ilium. Thus a thin, rigid shell of cortex surrounds the cancellous bone giving it the necessary strength but retaining the advantage of rapid revascularization.

Having planned a procedure designed to give a good anatomical and functional result, it is necessary that the surgeon insure its attainment. Many times it is seen that such planning goes to naught at surgery because of the impossibility of being absolutely certain that complete and full correction is obtained. Furthermore, often after the position obtained is apparently satisfactory, by the time the wound is closed, and the cast applied, the position of the fragments is markedly altered. For these reasons some modification of a tibial lengthening device should be used in the cases

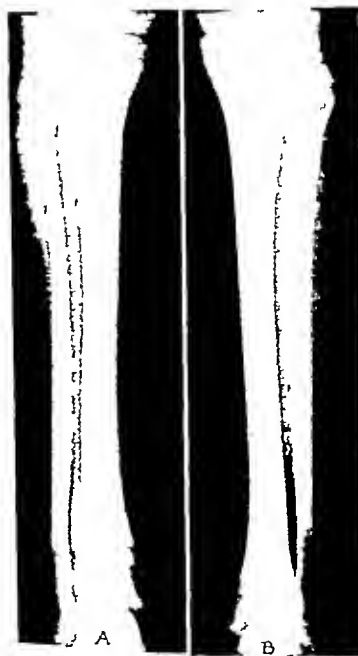


Fig 8 Teleroentgenograms taken on January 23, 1940, 13½ months after operation. Shortening of three-quarters of an inch still present.

in which marked deformity and shortening are present. It should be so designed that it can be applied under sterile conditions at surgery holding the correction under full view, and allow adjustment after operation with careful radiological control. This was done with great success by Morris and Downing and in the case reported in this paper.

Lengthening of the tendinous structures is suggested in the more advanced cases. The interosseous ligament should be divided as it will tend to restrict movement of the fragments toward correction. In these cases the anterior and posterior tibial tendons are very short and should be lengthened to give easy correction of the deformity.

#### CONCLUSIONS

1. Adduction injuries in growing children, resulting in fracture-separation of the medial malleolus may lead to premature cessation of growth in the medial portion of the distal epiphyseal plate of the tibia. Continued growth from the uninjured lateral portion produces a varus deformity and a shortening of the tibia.

2. The surgeon treating this type of fracture should insist upon careful follow-up and repeated x ray examinations until it is certain that no disturbances of growth may result.

3. If deformity is seen to be developing fusion of the distal epiphysis of the fibula and the lateral growing portion of the epiphyseal cartilage plate of the tibia of the affected leg should be performed immediately. This should be accompanied by closure of the distal epiphyses of the tibia and fibula in the normal leg in order to maintain equality in final length of the tibiae.

4. In the well developed deformity in growing children, correction must include closure of the lower epiphysis of the fibula and the lateral portion of the distal epiphyseal cartilage of the tibia of the affected leg to prevent recurrence of the deformity. This should be accompanied by fusion of the distal epiphyses of the tibia and fibula of the normal leg to prevent further inequality in the length of the tibiae.

5. Correction of the deformity can best be accomplished by a low oblique osteotomy passing through the area of the curvature. The wedge should be opened on the medial side. Ilac bone is suggested as a convenient and advantageous material with which to fill in the wedge.

6. In the severe cases division of the interosseous membrane between the osteotomy sites,

and lengthening of the anterior and posterior tibial tendons is advised.

7. In the cases with severe deformity a lengthening device is suggested as a method of insuring full correction as planned.

8. Equalization of inequalities in the length of the tibiae already present may be accomplished by closures of the appropriate epiphyses.

#### BIBLIOGRAPHY

1. ARTHUR A. P. End results of fractured distal tibial epiphysis. *J Bone & Joint Surg.* 33A, 3: 685-691.
2. BALBAST. *Fehlbildungen nach traumatischer Epiphysenschädigung am distalen Unterschenkelende*. *Ztschr. f. orthop. Chir.*, 1913, 58: 1-86.
3. BRIDGES P. A. Epiphyseal separation fractures. *Am. J. Roentgenol.*, 1913, 33: 58.
4. BROCKMUIR. Quoted by Poland.
5. BROCKMUIR, R. P. Discussion on Fractures in the region of the ankle joint. *Proc. Roy. Soc. Med.* 1914, 7: 201.
6. BUCKLEY, C. G. Deficient development of the lower end of the tibia after transverse fracture. *Lancet*, 1904, 361.
7. BURROWS, H. J. Brockman's operation for talipes varus resulting from defective tibial growth. *Proc. Roy. Soc. Med.* 1917, 30: 307.
8. CHAMBERLAIN, E. L. Growth arrest in long bones as result of fractures that include the epiphysis. *J. Am. Med. Ass.*, 1915, 65: 2140-2146.
9. DAVIES-COLLIER. Discussion on Injury to lower epiphysis of ulna. *Brit. M. J.* 1913, 600.
10. ELLIOTT, R. C. The relationship of fracture of the lower epiphysis of the tibia to arrest of growth of the bone. *J. Orthop. Surg.* 9: 4.
11. HAAR, B. L. The localization of the growing point in the epiphyseal cartilage plate of bone. *Am. J. Orthop. Surg.* 9: 7: 5: 583-586.
12. IDELL. The changes produced in the growing bone after injury to the epiphyseal cartilage plate. *Am. J. Orthop. Surg.*, 9: 6: 67-99: 66-170.
13. McFARLAND, B. Traumatic arrest of epiphysal growth at the lower end of the tibia. *Brit. J. Surg.* 1913, 9: 78-83.
14. MORRIS, R. H. and DOWNING, F. H. Report of case of vertical fracture through lower tibial epiphysis during period of bone growth and operation for correction of resultant deformity. *New England J. Med.* 1916, 5: 373-377.
15. MOUTRIER, C. M. Uncommon consequence of severe sprain of the foot. *Clin. Soc. Trans.* 1904, 30: 15.
16. OLIVIER, L. *Traité des résections*. Paris: G. Masson, 1903: 473-479.
17. OWICK, EDWARD. Cases of injury to the epiphyses, arrested development of tibia. *Lancet*, 1911, 747.
18. POCOCK, J. *Traumatic Separation of the Epiphyses*, pp. 846-851. London: Smith, Elder & Co. 1903.
19. ROSE, WILLIAM. Discussion on Injury to lower epiphysis of ulna. *Brit. M. J.* 1913, 600.
20. SMITH, M. K. The prognosis in epiphysal bone fractures. *Ann. Surg.*, 1914, 70: 373-376.
21. VAN AMBERG, J. *Mittheilung des distalen Unterschenkelendes nach Schädigung der Epiphysenflächen*. *Ztschr. f. orth. Chir.* 1914, 60: 454-460.

# FRACTURES OF BOTH BONES OF THE FOREARM IN CHILDREN

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**S**HAFT fracture of both bones of the forearm is not an uncommon injury among children, particularly in the younger age group. From the standpoint of both function and cosmesis the treatment of such fractures is important. Only by a careful examination of the end-results in a series of these cases can the relative merits of different forms of treatment be judged.

With this purpose in mind all shaft fractures of both bones of the forearm in children 16 years of age and under, treated in the outpatient department and wards of St. Luke's Hospital during the 7 year period from 1932 to 1938 inclusive, have been critically analyzed.

There were 50 patients in this series. Males outnumbered females two to one. The average age was 9 years, but 31 of the children (nearly two-thirds) were aged 10 or under. Undoubtedly this young age accounts for the fact that in 15 patients, 28 percent of the group, the fracture of both bones was of the greenstick variety. The 35 other fractures were complete, of radius and ulna.

The right forearm was broken 24 times, the left 26. Direct trauma was the known cause of injury in only 1 case, trauma was indirect in 36 and not recorded in 13. In most instances the child "fell while playing." Only 3 fractures were compound. Overriding was present in 11 cases.

Colles' fractures and epiphyseal separations have not been included in this series. In all but 2 cases both radius and ulna were broken at approximately the same level. Four were fractured in the proximal third, 18 in the middle third, and 26 in the distal third.

The use of some form of general anesthesia was recorded in 21 patients. In 3 cases reduction was not required, in 2 cases reduction was performed without anesthesia, and in 24 cases anesthesia is not mentioned. Local anesthesia, so far as can be determined, was not used.

For immobilization, anteroposterior plaster splints were usually applied to include the wrist and palm but not the elbow. In 5 of the 11 cases in which there was overriding the splint was made to include the elbow, in the 6 others it is not recorded whether the elbow was immobilized. Some form of immobilization was maintained an

average of 4 weeks and the patient was discharged after an average period of 5 weeks following reduction, excepting 4 patients who were watched between 3 and 4 months. In only 1 case was it recorded that fluoroscopy was used during reduction, though the fluoroscope may have been used in the others.

Physiotherapy consisting of baking and light massage was used in about half the cases, though when it was commenced and how long continued could not usually be determined from the record.

Six children refractured both bones through the original fracture site: 1 at 5 weeks, 4 at 3 to 4 months, and 1 at 1 year.

## FOLLOW-UP

Of the whole group it was possible to trace 32, or 64 percent. Lapse of time and a shifting population account for the loss of the others from follow-up. In all but 6 of the cases followed the child was found only after an exhaustive personal search through a maze of public and parochial schools and tenements in 4 boroughs of the city.

This follow-up includes physical and x-ray examination as well as bilateral measurements of the forearm length and wrist circumference of each child and an inspection of the carrying angle. The average follow-up period was 5 years. No case has been included which was seen less than 1 year and 5 months after initiation of therapy. Several represent an end-result of more than 7 years.

Whipple and St. John, in reporting the results of fracture of both bones of the forearm in 86 children 15 years of age and under, who were followed for an average of 18 months, concluded that open reduction of such fractures is unnecessary. Bagley more recently, in reviewing 176 similar cases, came to the same conclusion.

The results in this series of cases from St. Luke's Hospital accord with their findings. There were no clinically bad results among the patients personally followed. In no case did shortening of the forearm occur, and in only one case was there a demonstrable decrease in the carrying angle, this was in a child who had subsequently been treated in another hospital for refracture of the same forearm. In but 2 cases was there a differ-



Fig. 4, W.J.I. aged 3 years. Radius displaced and overriding. Double fracture of ulna. b, Closed reduction within 1 hour of injury. Still has 66 per cent displacement of radius and oblar angulation of ulna. Result at 3 years.

ence in the circumference of the two wrists. In both the fracture was within 2 inches of the distal epiphyseal line with an increased wrist circumference of 1/2 inch in one case and 3/4 inch in the other on the affected side. All three compound cases healed *per primam*. No complications resulting from the administration of anesthesia were recorded.

#### CLOSED REDUCTION

Unless one is familiar with the excellent ultimate results ordinarily obtained by conservative



Fig. 5, V.C. aged 5 years. Closed reduction soon after injury. There is still 75 per cent dorsal displacement of the distal fragments of both bones. b, Result at 4 years and 4 months. No evidence of displacement remains.

angulation of the ulna has disappeared. Displacement of the two sections of the radius has ceased. Moderate volar bowing which is barely perceptible upon clinical examination.

treatment of this fracture in youngsters, his natural dismay at failure to secure 100 per cent anatomical reposition of fragments on attempted closed reduction is very apt to force him into an unnecessary operative procedure. As a matter of fact it is surprising how often a good reduction can be obtained by simple manipulation even in the presence of marked displacement of both bones. Furthermore in contrast to adults, children exhibit a phenomenal capacity to re-establish the normal length, alignment and continuity of fractured bones even when there is gross displacement (Figs. 1 and 2) and overriding (Fig. 3) after reduction and immobilization have been carried out.

Twenty five patients treated by closed reduction were followed. Both anatomical and functional results were excellent in 11. Of the 4 children remaining 2 had good anatomical results with excellent function in one and fair in the other, 1 had a fair anatomical result with good function, and 1 patient had only a fair result both anatomically and functionally. This last is the child who sustained the decreased carrying angle mentioned. She had had a refracture of both bones treated in another hospital 1 year after the primary fracture and over 4 years preceding this follow-up.

The x-ray results in this group of closed reductions were excellent in 22, good in 3, and fair in 3. Solid bony union was demonstrated in every case. In no case did cross union occur between radius and ulna.



Fig 3 a, R S, aged 13 years Third attempt at closed reduction within 24 hours of injury Complete displacement and overriding of distal ulnar fragment persists b, Result at 7 years and 4 months No perceptible defect

#### OPEN REDUCTION

So satisfactory are the results of conservative treatment of these fractures in children that operative interference need rarely be employed. Actually, 4 patients in this series were subjected to open reduction, an operative rate which is admittedly too high. In 2 cases simple replacement of fragments under direct vision was performed. In a third case the ulnar fragments were fastened with a loop of wire passed through drill holes in the bone and in the fourth case similar fastening was accomplished with chromic catgut.

All 4 patients were followed. One had an excellent anatomical and functional result, 2 had a good anatomical result with excellent function, and one obtained a good result anatomically and functionally although he had non-union and pseudarthrosis of the ulnar mid-shaft, which could not be detected clinically.

The x-ray results of open reduction were good in 2 cases, fair in another and bad in the fourth. Cross union between radius and ulna did not occur and bony union was obtained in 3 cases. The fourth, classed as a bad x-ray result, shows non-union of the ulnar mid-shaft with a pseudarthrosis, though the radius is solidly united. As a result of this review it is now felt that all 4 open reductions could probably have been avoided, with ultimate results in every way at least as satisfactory as those obtained.

#### SUMMARY

1 During the 7 year period from 1932 to 1938 inclusive, 50 children aged 16 years and under were treated in the outpatient department and wards of St. Luke's Hospital for shaft fractures of both bones of the forearm.

2 Of these, 32 were personally examined and roentgenographed at an average of 5 years following injury.

3 Twenty-five of the 32 were treated by closed reduction with excellent anatomical and functional results in 21 and no bad result.

4 Four were subjected to open reduction with satisfactory results in 3 cases and a good clinical result in the fourth despite a non-union and pseudarthrosis of the ulna.

#### CONCLUSIONS

In children with shaft fractures of both bones of the forearm, complete anatomical reduction with end-to-end apposition of the fragments is not essential to excellent functional and cosmetic recovery. Open reduction of such fractures in children is rarely indicated.

#### REFERENCES

- 1 BAGLEY, C. H. Fracture of both bones of the forearm. *Surg., Gynec. & Obst.*, 1926, 42, 95-102.
- 2 WHIPPLE, A. O., and ST. JOHN, F. B. Study of 100 consecutive fractures of the shafts of both bones of the forearm. *Surg., Gynec. & Obst.*, 1917, 25, 77-91.



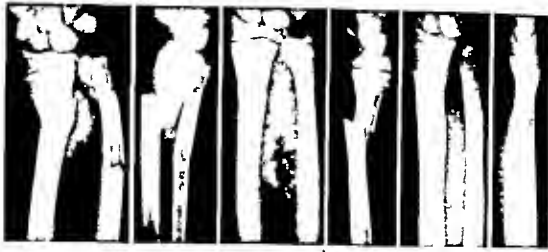


Fig. 4, W.M. aged 3 years. Radius displaced and overriding. Double fracture of ulna. b, Closed reduction within hour of injury. Still has 66 per cent displacement of radius and 60 per cent angulation of ulna. c, Result 1.5 years.

Angulation of the ulna has disappeared. Displacement of the radius sections of the radius has ceased. Moderate volar bowing which is barely perceptible upon clinical examination.

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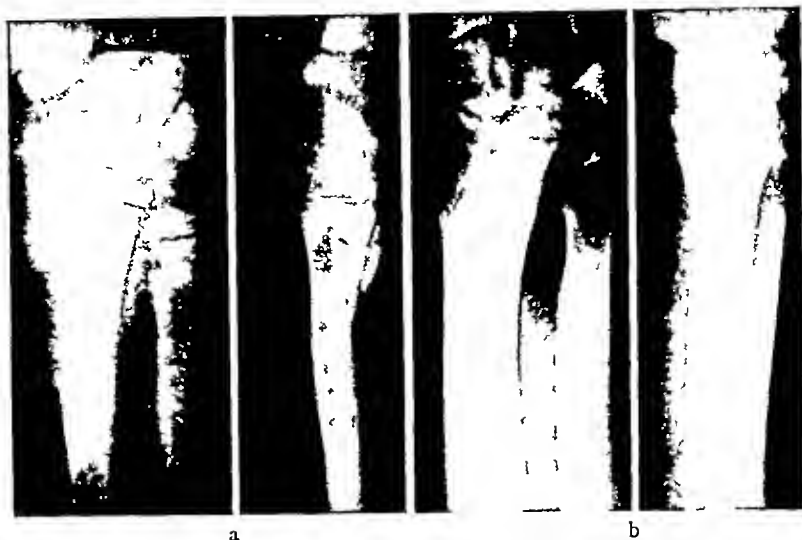


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# EDITORIALS

## SURGERY Gynecology and Obstetrics

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MARCH, 1941

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### VITTORIO PUTTI

THE Editors of SURGERY GYNECOLOGY AND OBSTETRICS announce with regret the death on November 1 1940, in Bologna Italy of Professor Vittorio Putti, one of the great orthopedic surgeons of the world.

Professor Putti was born March 1 1880. In 1914 he succeeded Professor Codivilla as director of the Istituto Ortopedica Rizzoli and during the first world war was chief surgeon at the Institute. He founded the periodical, *La Chirurgia degli organi di movimento* and was one of the founders of the International Society of Orthopedic Surgery and Traumatology.

Professor Putti gave several lectures in the United States—the last in 1933 at the meeting of the American College of Surgeons in Chicago when he discussed the subject of bone lengthening. He was honored in many countries for his outstanding abilities as a surgeon and teacher.

## A DECADE OF CONSERVATIVE TREATMENT OF INTESTINAL OBSTRUCTION

IN the past decade there have been two notable contributions to the treatment of intestinal obstruction (a) decompression of the distended bowel and (b) an appreciation of the physicochemical changes incident to high intestinal obstruction. Collier states that decompression is the greatest single technical contribution to abdominal surgery of the past ten years. Without doubt, the credit for putting this form of treatment on a rational basis belongs to Wangensteen.

Until a few years ago it was generally admitted that there had been very little progress in reducing the mortality of acute intestinal obstruction. Besides the paroxysmal administration of fluid and electrolytes, the treatment consisted chiefly of enterostomy with or without release or removal of the obstructing mechanism. The average mortality from these surgical procedures was from 40 to 100 per cent depending upon the duration and nature of the obstructing lesion, the condition of the patient, and the surgical procedure performed.

Conservative therapy in cases of ileus consists of saphonage drainage to an indwelling intestinal catheter (Wangensteen or Miller Abbott tubes), proper fluid and electrolytic balance, judicious sedation, and above all an appreciation of the limitations and indications for this method of treatment. Fine has suggested the inhalation of 95 per cent oxygen to relieve the gaseous distention in intestinal obstruction. This is a valuable adjunct but the best results are obtained when combined with saphonage drainage of the bowel.



There is much to be learned, however about intestinal obstruction. The diagnosis of the type of ileus is of paramount importance and depends upon a close correlation of the history, physical examination, and roentgen-ray findings. At times it is difficult to differentiate between a strangulating obstruction and a simple mechanical ileus, but all agree that such patients should be operated upon. The mortality of operations for strangulating obstruction is far from ideal. Better surgeons have a lower mortality for gastric resection than for strangulating obstructions of the gut. It will be interesting to see what progress will be made in the next decade in the treatment of ileus.

CHARLES E. REA.

## WAR SURGERY

**G**REAT emergencies arouse men and nations to great effort. If there is any compensation for the tragic destruction of lives, of property and of ideals that results from war it must be found in the greater tolerance and kindness that come from sharing common privation and danger and the inventions that are born of dire necessity.

Every war from the beginning of time has stimulated interest in surgery but, too often, when the war has ended, the hard won lessons have been forgotten. Now again, papers on war surgery are finding their way in increasing numbers into surgical literature and soon, doubtless, demands for "short courses" in war surgery will be made on medical schools, clinics and medical groups.

Under the guidance of an illustrated press and of vivid portrayals of scientific progress skillfully dramatized by laymen for laymen it is easy to visualize "war surgery" as something new and fascinatingly different from the prosaic surgery of civil life. As a matter of fact it differs only in one respect—that large

numbers of seriously injured individuals suddenly confront the surgeon, demanding skillful and efficient care.

To cover open wounds with sterile dressings, to immobilize injured extremities, to relieve pain with sedatives and administer antitetanic serum, and then to transport wounded men rapidly and safely to surroundings where they can receive surgical care are essentially problems of organization. To work out such organization demands the best thought available to execute the plan requires only intelligence, co-operation and elementary training, not prolonged medical training.

When the wounded patients reach a surgical center again it requires the keenest diagnostic ability to determine which patients demand immediate attention, which can wait for a few hours, which can be evacuated with minimum risk. The important consideration is that actual surgical treatment, once begun should be the same treatment accorded the man injured in a factory in a home, or on Michigan Boulevard.

In recent years we have often heard the terms "industrial surgery," "traumatic surgery," "office surgery," etc. and have not heard often enough the term "good surgery." There is only one type of surgery that deserves emphasis—the good surgery that the injured patient requires, no matter where or how he may have been injured. There must be one best method of treating a compound injury and that method cannot be learned in short "refresher courses" but only from teaching and demonstration in medical school, from first hand observation and practice in hospital internship and residency and finally from persistent and conscientious application of sound surgical principles in daily practice.

War does drive home some simple lessons and basic principles that are too often neglected in medical school and hospital because

of the lure of more appealing tasks. There is no new magic in petrolatum and plaster, but there is magic in undisturbed rest and freedom from exposure to the constant re-infection too often introduced into open wounds by careless fingers and droplets from uncovered mouths and noses. There is no new magic in hasty excision of devitalized wound edges and immediate closure of an open wound, perhaps after filling it with sulfanilamide crystals. There

may be some magic in laying sulfanilamide crystals under the occluding dressing of an open wound that cannot be surgically treated immediately after injury, so as to produce temporary bacteriostasis, but the real magic lies in transforming contaminated wounds into clean surgical wounds in the simplest possible way and without mechanical or chemical trauma of the living tissue upon which healing depends.

SUMNER L. KOCH





Fig 1 Reproduction of a fifteenth century painting "Médecin urologique dans son cabinet," showing urologist and patient. Courtesy Burroughs Wellcome & Company

are given concerning white, green, yellow, black, red, and leaden colored urines. Special chapters pertain to cloudy urines or those with sediments and granular deposits and odor of urines. In many of these prognostications the patient is adjudged suffering from anorexia, dyspepsia, clogged liver (?), weakness of the extremities, all common to many different ailments.

At any rate, urine divination or uroscopy was attacked in no uncertain terms directly or by telling sarcasm which latter method is often more effective than the best developed logical and scientific argument.

The most amusing story exemplifying the latter type of attack is told of the illustrious and arrogant Dr Radcliffe (1650-1714), who was known not only for his medical skill but also for his plainness and coarseness and who was nevertheless an early possessor of the famous *Gold Headed Cane*<sup>1</sup>, a book which every medical man should read.

It is stated that on one occasion a woman called on this famous doctor with a urine glass or receptacle similar to the one here represented (Fig 1), and dropping a curtsy asked him to determine the nature of her husband's illness and

to prescribe for his relief, the patient being 4 miles off. Dr Radcliffe asked for the vessel and after looking at it inquired of the patient's trade. On learning that he was a bootmaker the doctor retired for a moment with the urine glass and after emptying its contents and replacing it with a more recent sample of urine, returned it to the anxious cobbler's wife with a statement to the effect that if her husband would undertake to make for him, Dr Radcliffe, a proper pair of fitting boots he would prescribe for him and his "distemper" by a similar examination.

It was Dr Willis who excoriated the uroscopists of his time in these words in chapter VI, of his work already referred to, as well as the initial paragraph of chapter VII where he writes as follows —

"These were what I had to say concerning the Judgments of Urine not collected from the vain Traditions of Quacks but what are consonant to reason and truth. Besides I know there are ordinarily delivered by Medicasters and Old-Women almost an innumerable company of Rules and Directions of Urine-Divination that the urinal is no sooner suspected but they will undertake to divine, whether the Patient be subject to the Passions of Love or Sadness, whether a Woman hath conceived with child or not, or whether it shall be a Boy or a Girl and an hundred other the like, in which using a vain conjecture, they either

<sup>1</sup>The Gold Headed Cane. By William MacMichael. First published in 1828 and republished many times and most recently by Paul Hoeber Inc., New York, 1926.



impose by their confidence on the minds of the credulous, or (which is more frequently their custom) by a cunning craftiness they other ways sift out the matter by inquiring and falsely ascribe it to their knowledge in the inspection of Urine." And "although the business of the Examination and Inspection of Urines seems commonly only a simple thing (*viz.* the Medicastrs and Quacks for the most part behold the Urine sent in a Glass, shake it a little and presently give Judgment) yet to those who honestly endeavor the recovery of the sick the matter seems a little more intricate and they use to observe several circumstances covering Judgment by Urine which being omitted, nothing indeed can be certainly or directly learnt in the Medicinal Practice for the Urinal."

Fohn<sup>1</sup> who centuries later became the Father of modern urinalysis was anticipated by Willis who recognized that a knowledge of the volume color consistency and content of sound urines was necessary before attempting to investigate the quantity and color of "sick peoples urines," which

Willis describes. His analysis, however is but a variant of the so-called "apagryic analysis of Paracelsus. It is curious that in this exposition no mention is made of his own discovery of the sweet character of the urine of some diabetics made seven years previously ("Cur autem *Insar sacchari*, aut *mellicis* ex *miſce dulcorat*, *notis vinctice dignus est*)<sup>2</sup>

As for the rest, Willis was aware of the fact that he had contributed very little for he ends his treatise on urines, thus

And thus, Sir at length you have the Doctrine or Method of Separation of Urine, such as our unskillfulness hath rendered it. I desire you would be pleased not only to pardon the errors and bareness of this Discourse, but also to excuse it in other things, because at first writ by your persuasion, and then by your command and request made publick. Wherefore pray take care of this child hardly brought forth and almost so abortive, and as it were exposed and deservedly laid at your door without portion. Farewel.

*Thermaceutica Rationabla.* By Thomas Willis, M.D. 1649. Serie IV. Cap. III, De Diabete, p. 117

<sup>1</sup>Fohn, O. Approximately complete analysis of thirty normal urines. *Ann. J. Physiol.* 1901, 3, 45 and Laws governing the chemical composition of urine. *Ibid.* p. 66.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE work entitled *The Therapeutics of Internal Diseases*<sup>1</sup> edited by Blumer is to be published in four volumes, the first two of which are reviewed herein. Appreciating the difficulty in editing a work on an ever changing subject such as therapeutics, Dr. Blumer states, "Any work on therapeutics can only attempt to cover the subject as it exists at present." Nevertheless, an excellent, broad groundwork has been laid and probably will require little change in the future. Volume 1 covers the principles of therapeutics, discussing extensively the various phases of physiotherapy, nutrition and dietetics, endocrine, serum and vaccine therapy, and the principles underlying nonspecific therapy and bacteriophage. In the chapter discussing the principles underlying treatment in psychiatry, there is some duplication of subject matter taken up in previous chapters. Section 2 includes special therapeutic technique, beginning with oral medication and prescription writing and ending with rectal, parenteral, intradermal, hypodermic, intramuscular, and intravenous medication. There are also chapters on blood transfusion, spinal puncture, and paracentesis.

Like most symposia there is great variation in the discussion of the numerous subjects. Dr. Barach's contribution discussing the use of gases is particularly noteworthy. The book is well printed in easily readable type. If the subsequent volumes follow the same general plan as the first two there is no doubt that this work will become a valuable contribution.

J ROSCOE MILLER.

THE picture of a kindly, lovable, skillful surgeon with a happy faculty for making warring factions and individuals forget their differences and work in harmony, illuminates the pages of Finney's interesting, very readable and often amusing *Life of a Surgeon*<sup>2</sup>.

The biographer in writing his own life story is handicapped (though not all biographers have been so restrained) by an innate modesty, and the desire not to say unkind or critical words about anyone, whether still living or long since passed into the great beyond. This restraint detracts perhaps from the color and vividness of a story which covers an important period in American medical and national history, and which brings to life again Princeton in the eighties, the Harvard Medical School and the

Massachusetts General Hospital of Maurice Richardson, Arthur Cabot, Homans and Porter, Fitz, Scudder and J. Collins Warren, the beginnings of the Johns Hopkins Hospital and Medical School, and, years later, the Great War. Great figures of the past troop by in an interesting array, and no medical man whose training and service began or ended during the half century of the author's active surgical career but will be interested in this panorama of events and personalities.

To the reviewer the most arresting pages are those in which the author pays tribute to Halsted, Welch, Osler, Thayer, and Walker—contemporaries and colleagues, with whom he lived and worked through so many stirring years. Here he can throw aside restraint and express himself with the enthusiasm and fervor of which he is capable. His portrayal of Halsted in particular makes "The Professor" live again, and persuades the reader that he can visualize and understand this distinguished teacher of surgery, though he never had the opportunity of studying under him or seeing him at work. Altogether the volume is a welcome addition to the annals of American surgery and will be treasured as such by all who read it.

SUMNER L. KOCH

THE purpose of the authors, Meyer and Oscar Bodansky, in writing *Biochemistry of Disease*<sup>3</sup> was to provide a "systematic presentation of the biochemical aspects of the various diseases, arranged according to clinical entities." To the reviewer's knowledge, there is no other book on biochemistry which is arranged and presented in this way, so that the biochemical aspects of any particular disease may be found under its specific heading.

The book is divided into eighteen chapters, each dealing with a particular group of diseases. It starts with a chapter on diseases of the blood, followed by one on diseases of the heart, a third on diseases of the digestive tract, while diseases of the kidneys and urinary tract are combined in one chapter as are diseases of the liver and biliary tract. Each of the endocrine glands is accorded a separate chapter. The last five chapters are devoted to diseases of bone, of muscle, disorders of metabolism and nutrition, and diseases of the nervous system.

By eliminating long theoretical discussions and including only those aspects of biochemistry which have a direct clinical application, the authors have made available a practical aid in diagnosis, prognosis, and treatment.

<sup>1</sup>THE THERAPEUTICS OF INTERNAL DISEASES. Edited by George Blumer, M.A. (Yale) M.D. With the assistance of Albert J. Sullivan M.D. Vols. 1 and 2. New York and London: D. Appleton-Century Co., Inc., 1940.

<sup>2</sup>A SURGEON'S LIFE: THE AUTOBIOGRAPHY OF J. M. T. FINNEY. New York: G. P. Putnam's Sons, 1940.

<sup>3</sup>BIOCHEMISTRY OF DISEASE. By Meyer Bodansky, Ph.D. M.D. and Oscar Bodansky, Ph.D. M.D. New York: The Macmillan Co., 1940.

They have presented a very thorough review of the literature, and extensive bibliographies at the end of each chapter enable the reader to consult the original sources. However, being a review of the literature, it has the unavoidable shortcoming of being not completely up-to-date in certain instances.

Rarely are significant references omitted from the extensive bibliography.

The easy flowing style makes the presentation like the lectures of an experienced teacher. This volume should be popular with practitioners and students alike.

M. HERBERT BAKER

## BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

A TEXTBOOK OF CLINICAL NEUROLOGY. By J. M. Nielsen, B.S., M.D. F.A.C.P. New York, London: Paul B. Hoeber Inc. 941.

TRANSACTIONS OF THE SIXTY-FIRST MEETING OF THE AMERICAN SURGICAL ASSOCIATION HELD AT WASHINGTON UNIVERSITY ST. LOUIS, MO. MAY 1, AND 2, 1940. Vol. 58. Edited by Walter Estell Lee, M.D. Philadelphia: J. B. Lippincott Co. 940.

RADIOLOGIC PHYSICS. By Charles Weyl, S. Reid Warren, J., and Duffett B. O'Neill. Springfield, Ill. and Baltimore, Md.: Charles C. Thomas, 941.

THE ROLE OF THE LIVER IN SURGERY. By Frederick Flisshert Boyce, B.S., M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 941.

THE PHARMACOLOGICAL BASIS OF THERAPEUTICS. By Louis Goodman, M.A., M.D. and Alfred Gilman, Ph.D. New York: The Macmillan Co. 941.

THE PRACTITIONER'S LIBRARY OF MEDICINE AND SURGERY. 940 Supplement. New York and London: D. Appleton Century Co., 941.

THE EXTRA-OCULAR MUSCLES. By Lester C. Peter, A.M., M.D., Sc.D., LL.D. Philadelphia: Lea & Febiger 941.

WILLIAMS OBSTETRICS. By Henrick J. Stander, M.D. F.A.C.S. New York and London: D. Appleton Century Co., 941.

EMERGENCY SURGERY. By Hamilton Bailey, F.R.C.S. (Eng.) Baltimore: The Williams & Wilkins Co., 940.

A CIRURGIA CONSERVADORA NAS NEFROPATIAS (Cirurgia Médica). By Dr. Rodolpho de Freitas. São Paulo, Brazil: Livraria Triunfante, 940.

LA RADIOGRAFÍA PENETRANTE DEL TÓRAX. By Benjamín Enquist and Juan Alberto Aguirre. Buenos Aires: El Ateneo, 940.

ANUS, RECTUM, SIGMOID COLON; DIAGNOSIS AND TREATMENT. By Harry Elliott Bacon, B.S., M.D., F.A.C.S. F.A.P.S. Philadelphia, Montreal, and London: J. B. Lippincott Co. 941.

AGE MORPHOLOGY OF PRIMATE TENDONS. By Henry C. Sponky, M.D. Springfield, Ill., and Baltimore, Md.: Charles C. Thomas, 1941.

THE AMERICAN COLLEGE OF PHYSICIANS: ITS FIRST QUARTER CENTURY. Histories: William Gerry Morgan, M.D., LL.D., Sc.D. M.A.C.P. Philadelphia: American College of Physicians, 940.

## CORRESPONDENCE

### VALUE OF RADIATION THERAPY IN THE TREATMENT OF CARCINOMA OF THE BREAST

To the Editor: A paper of mine entitled "The Value of Radiation Therapy in the Treatment of Carcinoma of the Breast" was published in volume 62, of SURGERY GYNECOLOGY AND OBSTETRICS, in April, 1936, p. 653. It has just been brought to my notice now that the averages given in the various tables in that paper are statistically invalid, since it would appear that for correct averages, count would have to be taken of the numbers of cases comprising

the various groups averaged. As I am neither mathematician nor statistician, I was not alive to this point, which must also have escaped the editorial staff.

Although this does not impair the interest of the other figures and observations, conclusions that depend upon comparisons of average figures are not proved. After all these years, it is difficult to make correction, but I should be happy if in the interests of scientific accuracy you could publish notes to this effect.

R. G. HUTTON

Radiologist Royal Alexandra Infirmary  
Paisley Scotland

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### EXPERIMENTAL ANALYSIS OF THE GROWTH PATTERN AND RATES OF APPositionAL AND LONGITUDINAL GROWTH IN THE RAT FEMUR

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THE problem of bone growth has been studied for centuries and to the present day is not completely understood. From the earliest records, information has been gathered from purely morphological studies. The chief advances in the knowledge of bone growth have been made using the physiological method of vital staining. The purpose of this study was to investigate experimentally the growth pattern and assess quantitatively the rates of growth in long bones by the method of vital staining.

#### REVIEW OF LITERATURE

The foundation of our knowledge of the mode of bone growth began in 1736 when John Belchier (16), an English surgeon, was entertained at a dinner by a calico printer. The entree was roast pig and a joint of this pig was served to Belchier. The pink, ruddy color of the bones of this pork aroused the scientist's curiosity and he asked his host about the origin of the pig. The calico printer, being an economical man, used the madder-soaked bran from his dye vats to feed his pigs. The pigs he then used to feed to his friends. Subsequently, Belchier fed madder root to a cock forcibly

and it died in 16 days. This single result of the pink color of the fowl's bones, he reported to the Royal Society (3).

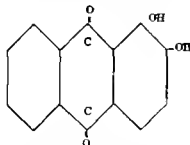
Henri Louis Duhamel fed madder to animals and then withdrew the dye. He observed that upon later sacrificing the animal, nearly all the redness was gone from the bone. This led him to believe that the stain was only temporary. When these bones were sectioned, he observed that the madder colored layer was covered and hidden by an unstained surface layer of bone laid down after the madder diet had been suspended. Duhamel then found by alternating madder diet with periods without madder he obtained red and white layers on the circumference of the bone. The last formed layer or plate was on the surface of the bone immediately under the periosteum. He concluded that bone grew as wood grew with superposition of layer upon layer. He also concluded that it was the periosteum that possessed the osteogenic function.

This method of vital staining with madder was not new although it was noticed by Belchier in 1736. It was known to the Greeks (11). The Egyptians brought madder from India where they learned the trick of combining it with calcium, aluminum salts, and polymerized fatty acids as mordants (18).

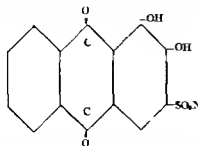
From the Division of Surgery, Northwestern University Medical School. Awarded the Chicago Surgical Society Prize for Research Completed in 1940.

Madder is a powdered root of *Rubia cordifolia* in India and Central Asia. In Europe it is the *Rubia peregrina* (native wild plant) of England, Wales, and Ireland. The U S Dispensatory refers to it as *Rubia tinctorum* (23). The active principle of the madder root dye is alizarine and purpurin and its name was received from the trade name Levantine madder root (4). The dye occurs as a glucoside (ruberythric acid) in the roots in 2 to 4 per cent proportions and is obtained by fermentation or boiling with dilute acids. It is a reddish yellow powder insoluble in cold water and slightly soluble in boiling water. However it dissolves in hot alcohol, ether benzene glycerine, or glacial acetic acid.

Alizarine was isolated from madder by Robiquet and Colin in 1827 (5). Graebe and Lieberman in 1870 showed that it was a glucoside of the anthraquinone type, 1-2 dihydroxyanthraquinone.



Perkin (17) 1870, found the sodium sulphate salt, alizarine red S which was more soluble and more stable than alizarine.



Alizarine has a varied tinctorial gradient depending on the hydrogen ion concentration of the medium. At hydrogen-ion concentration 5 it is yellow at hydrogen ion concentration 5 to 6.8 red and at hydrogen-ion

TABLE I.—EXPERIMENTAL HISTORY OF 52 ALBINO RATS GIVEN INJECTIONS OF ALIZARINE RED S FROM 11 TO 299 DAYS OF AGE

Group No.	Arbitrary age range of animals in days	Number of animals allocated to each group	Age in days when injected	Interval between injections in days	Age when sacrificed
	10-30	20	7-14-18-66	7-14-47 9-13	22-52-66 54-67-75
	30-60		27-31-36-38 37	36-41-46 39-52-57	64-68-72 70-1 123
	60-90	14	7-14-27-76 42-67-82-90	14-21-47 42-64-6	90-1 97-111 124-154
	90-130		100-149-168 169-180-187 142-143	9-12-30 27-33-40 41-66	173 18-113 130-146 154-171 179 199
5	30-60		(63-104-173)	9-19-30 21-32-46	170-180 195
6	90-304		102-113-190	27-30 32-52-100	149-166 200-206

concentration greater than 6.8 it is purple (4). The younger the age of the animal injected, the deeper is the color of the stain in the bones and teeth while old animals take the stain poorly or not at all. Thus, there is a selective staining of bone and teeth which are growing and calcifying at the time of injection.

Hoffman (12) in 1939 demonstrated that the staining effect of alizarine red S in bones is dependent upon the hydrogen-ion concentration value of the colloidal matrix at moment the calcium precipitates to its earthy state.

Schour and Hoffman (13, 19-22) measured the appositional growth of the incisor and molar teeth in the rat, as demonstrated by alizarine red S. These workers injected the rat with alizarine red S at varying intervals and measured the amount of appositional growth over that given period. Their work opened a new field of research on growth of teeth and bones and directly suggested a similar study on rat femur.

#### METHOD AND MATERIALS

This study is based on the examination of 180 albino rats ranging from 7 to 304 days of age. Intraperitoneal injections of a 2 per cent isotonic alizarine red S solution, color index No. 034, were given at intervals of 7 to 101 days. The pharmacological dosage was

experimentally found to be approximately 100 milligrams per kilogram (Hoffman and Schour, 19) The macroscopic and microscopic measurements were based on 52 animals (Tables I, II, III, and IV) Intravenous injection allowed for too rapid excretion of the dye before it could be deposited in the ossifying bone

*Number of injections* On the basis of preliminary trial animals, it was found advisable to limit the number of injections to one or two for each animal since more than two lines caused confusion as to which injection produced which line For convenience, the animals were allocated into incremental age groups depending upon the days on which they were injected (Table I)

*Dissection and the preparation of microscopic sections* The usual method of making microscopic sections of bone for histological study by decalcification in acid could not be employed in this experiment since the red to purplish effect of the alizarine red S in the bone is decolorized Gross specimens were preserved in 10 per cent formalin to which magnesium carbonate had been added After the bone was cleaned of all muscular and tendinous attachments, cut sections were prepared at the following levels (a) through the neck and head, (b) transversely through the shaft, distal to the lesser trochanter, (c) transversely through the diaphysis, and (d) longitudinally, midsagittal mediolateral sections (Figs 1 and 2)

The bone was cut with a 0.5 millimeter jeweler's saw blade which was mounted in an appropriate frame One surface of the cut section was ground smooth on a circular fine grade carborundum stone attached to a laboratory lathe This section was dehydrated in alcohol and treated with acetone The smooth surface was fixed to the flat ground facing of a cork in cellulose cement The cement served as an embedding medium and to attach the section to the cork When the cement was completely set (4 hours), the exposed surface was ground to a thickness of 20 to 50 microns While being ground, the bone was continuously cooled and washed free of debris by a stream of water passing through a brush placed against the stone Final polishing of the section was completed on a hard Arkansas stone

The bone was removed from the cork by immersion in acetone Several changes in fresh acetone were necessary to free the sections of excess cellulose cement The sections were then dried and cleared for 24 hours in xylol and mounted in gum dammar It was found that the red stain faded and disappeared in several weeks from sections which were mounted in balsam One half of the longitudinal section of the femur was ground and mounted as described while the opposite half was immersed in xylol for clearing The cleared bones were examined with the aid of a binocular dissecting microscope while suspended in the clearing solution The red stain could be studied from a three dimensional aspect

*Method of examination* Gross specimens were measured for length and diameters overall with a Boley gauge Readings were made correctly to 1/100 of a millimeter

Microscopic studies of the ground sections were made under the 32 and 16 millimeter objectives A vernier filar micrometer eyepiece which was calibrated to a standard micrometer stage for the microscope and lenses, was used to make the measurements between the injection effects of the alizarine red S Measurements were made in microns and were calculated correctly to within the first decimal place

Measurements were made at the levels shown in Figures 1 and 2 The mean values, standard deviations, and error of the mean were calculated for the specific levels of animals within specific age groups (Table I)

The measurements of the means for each animal were plotted against time (Figures 5, 6, 7, 8), both arithmetically and logarithmically

#### FINDINGS

*Gross observations* Gross examination revealed a diffuse, purplish-red stain of the femur in animals injected with alizarine red S from birth to 15 days of age Animals injected at 15 days of age and sacrificed at 30 to 60 days of age presented a diffuse, purplish-red stain in the metaphyseal portions of the bone and a colorless diaphyseal bone as well as a colorless subcapital segment The junction of the colorless diaphysis with the shaft showed an intensely stained band which encircled the bone at that level (Fig 3, left) The longitudinally

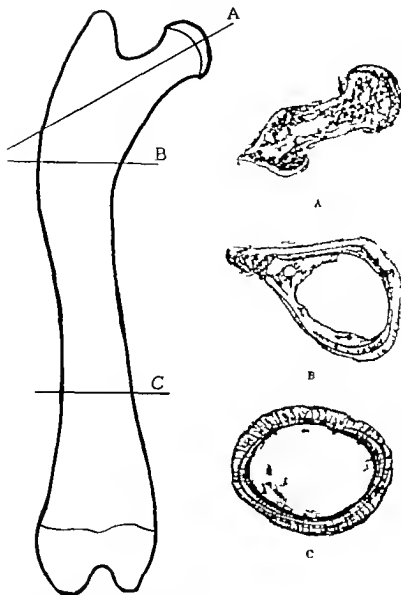


Fig. Photomicrographs of transverse ground sections and levels at which they are made through the femurs of alkalinized rats. *A* Longitudinal through head and neck and obliquely through the shaft distal to the greater trochanter. *B* Shaft, just distal to the lower trochanter. *C* Diaphyseal end of shaft.

cut section (Fig. 2) of the bone presented a diffuse red stain in the medullary cavity but the sharp differentiation between colorless diaphysis and stained shaft was not seen as a sharp line and faded gradually toward the distal end.

The circumferential colored lines on the surface of the cortex in the shaft of the bone were parallel to the epiphyseal plate and varied in their distance from the epiphyseal plate in

approximately direct relation to the number of days intervening between injections. The animals which were given injections at varied intervals presented parallel colored rings about the shaft, the distance between which was the amount of longitudinal growth at the diaphyseal ends of the bone for that interval.

The longitudinal midsagittal sections (Fig. 4) presented oblique red lines extending from the medulla of the shaft outward and toward

the epiphysis (Fig 3 and 4) to end tangentially at the surface of the bone with the parallel lines mentioned. This would be at the epiphysis if the animal were injected and sacrificed within a few days. When 10 to 30 days elapsed between an injection and the time the animal was sacrificed, these oblique red lines were found at a distance away from the epiphyseal plate and ended at the periosteal surface red line (Fig 4). This arrangement of a circular base with oblique lines beginning at the cortical margin and extending away from the epiphysis and medially formed a red truncated cone. The cleared femurs of animals which had been given one injection presented this picture in three dimensions when examined with a binocular dissecting microscope. When a second injection was given 30 days later the oblique red lines were found epiphyseally to the first line and were parallel to them. These oblique lines ended at the periosteal surface of the cortex where the red circular lines were found. The perimeter of the base of this cone formed the circumferential lines seen on the surface of the cortex (Fig 3). Each succeeding injection line was found epiphyseally to the previous one in the form of one cone within another. The base was the epiphyseal plate but as more bone was deposited, the legs and the perimeter of the cone (Fig 4) remained in the shaft as fixed planes. The base remained as the epiphyseal plate and did not take the alizarine stain.

Subsequent injections formed new cones which were seen to dovetail within the cones formed by the previous alizarine red S effects. The epiphyseal plate was now found to have receded from the levels of the initial alizarine red S rings (on the surface of the bone) and was approximately parallel to them.

*The neck.* Longitudinal sections through the neck (Fig 1, A) included an oblique section through the shaft and lesser trochanter. The oblique endosteal red lines passed from the marrow cavity of the neck upward and outward toward the capital epiphysis. The periosteal deposit was found about the neck and was continuous with the red line in the trochanter and shaft (Fig 1, A and 4). A morphological arrangement of the alizarine red S lines, similar to that of the distal end of the

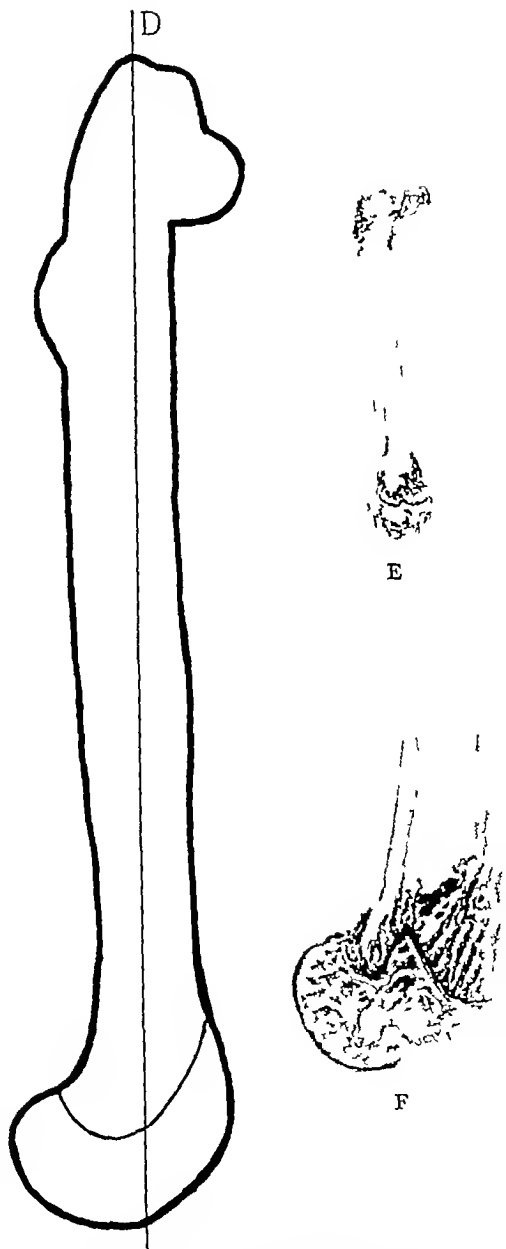


Fig 2 D, Longitudinal midsagittal section through shaft of the femurs of alizarinated rats. E, Mediolateral view. F, Anteroposterior view.

femur, existed in the neck. Similar truncated cones appeared superposed one within another excepting that the base was proximal while in the condylar end of the femur the base of the cone was distal.





Fig. 3. Photograph of the femur of 75 day old rat showing the effect of one injection of alizarine red S given at 87 days of age. Left, magnified longitudinal section of left femur showing alizarine red S effect in cortex. Right, Outer surface of the cortex of the right femur showing the alizarine red S effect at the proximal and distal end.

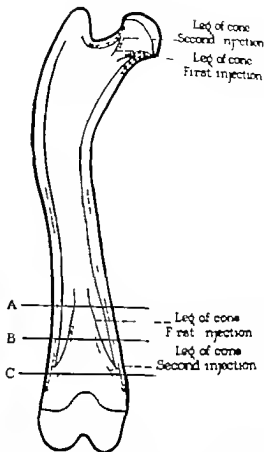


Fig. 4. Longitudinal section through femur showing alizarine red S effects in 50 day old animal. Solid line, first injection at 60 days of age. Broken line, second injection at 80 days of age.

**Periosteal growth.** Concomitant with the longitudinal growth of bone there was seen a subperiosteal deposition of bone about the entire shaft. This subperiosteal deposition of bone showed the alizarine red S effects. When viewed in cross section, circular red rings were seen to parallel the periphery of the bone. Cross sections through the shaft at the subtrochanteric level (Fig. 1 B) showed circular red lines in the cortex. The number of concentric lines at this level was directly representative of the number of injections given.

Transverse sections through the diaphysis presented three different findings dependent upon (1) level of diaphysis through which section was made (2) number of injections and (3) interval of time between injections.

When one injection was given one or two circular lines were found. When two injections

were given, two, three, or four concentric red rings were seen (Fig. 4 A B C). The distance between the lines was not regularly equal as those found in the subtrochanteric region of the shaft. To clarify the discrepancy in the number of circular red lines found in the diaphysis as compared with the number of injections given, it was necessary to restudy the cleared sections. The junction of the red line of the cone on the inner surface of the shaft with the periosteal deposit showed two lines on cross section (Fig. 5 C). The solid black line indicates size of bone at time of first injection. Broken line at second injection.

**Haversian bone.** The walls of the vascular channels in the haversian systems showed the

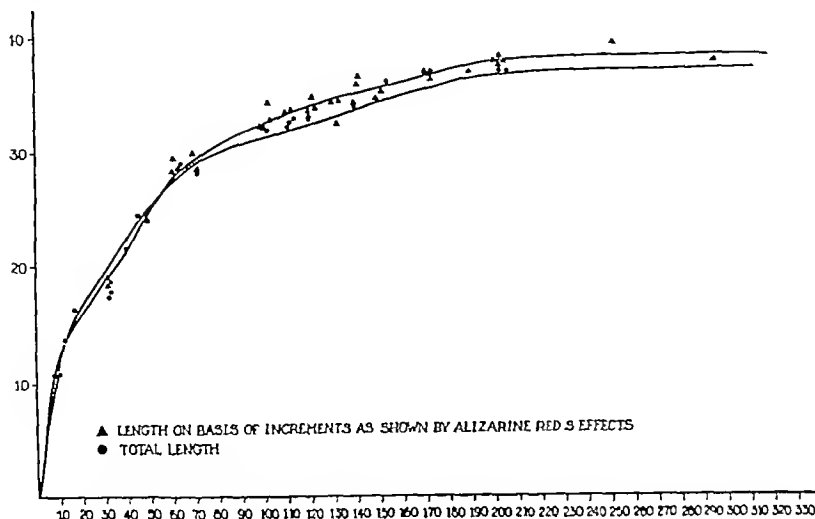


Fig 5 Graph showing total lengths in millimeters and total longitudinal increments as shown by alizarine red S effects in the femurs of 52 albino rats from 11 to 364 days of age (From Table II)

alizarine red S effects in the arrangement of concentric rings. The concentric lamellae of the bone cells were parallel to these red rings. Bone growth within the haversian systems occurred as a result of deposition of new bone on the wall of the vascular channel and

caused a diminution in the diameter of the channel.

#### QUANTITATIVE ASSESSMENTS

*Longitudinal growth — gross* The lengths over-all of the femurs on the basis of 10 day

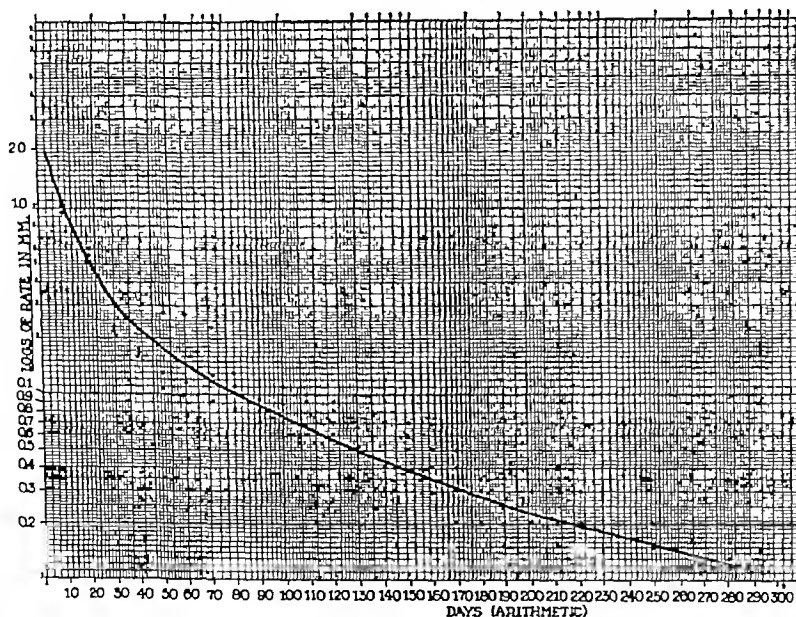


Fig 6 Graph showing semilogarithmic representation of the daily rates of longitudinal growth in the rat femur from 10 to 304 days of age

TABLE II.—TOTAL LONGITUDINAL INCREMENTS OF GROWTH IN THE FEMURS OF 52 ALBINO RATS FROM 11 TO 304 DAYS OF AGE

No. of rat	Age in days	Growth at distal end in mm.	Growth at neck in mm.	Length of femur in mm.	Age (in days)	Total length in mm.
			.04		28	28.6
13	40		.40	17	40	
30		.33	.80	10		
18		.90	.80	19.6		24
309			.13		.48	26.48
137	6	.00	.11	.44	.48	27.84
305	6.4	.84	.13	.44	.48	28.87
06	8.4	.6	.78	.98	.53	29.66
5	66	.80	.80	.44	.48	30.70
04	71	.94	.90	.44	.48	31.80
064		.01	.81	1.8.6	1.1	32.46
26	98	.08	.30	.08.17	7	33.08
79	09	.86	.30	.08.17		34.36
241	303	.86	.14	.48	6	34
208	192			.68	6	34.16
19	187	.30	.60	.00.17		35.06
		.06	.86	.79.19		35.96
130			.15	.31	.99	36.19
130		.78	.01	.01	.71	36.76
300	30		.48		.99	37.4
144			.11		.99	37.57
09		.23		.51	.99	38.60
06			.67	.09		39.80
160	39	.35		.31	.90	40.60
	.13	.97	.48	.31		41
304	130	.80		.57	.87	42.23
	.14	.04	.38	.31	.99	44.9
03	.14			.51	.90	46.17
	.14	.89	.47	.31	.90	46.66
14	.14	.15	.115	.31	.96	48.57
10	171	.80	.40	.34	.54	47.96
	.73	.40	.80	.33	.49	47.40
	173	.06	.66		1.00	48.19
78	203	.05		.35		48.46
139	205	.17	.30	1.5.8		48.46
19	205	.38	.90	.36	.94	50.79
138	205		.58	.36	20.3	51.69
06	.68	.78	.86	.37	20.6	52
79	207	.443	.06	.37	20.6	52

TABLE III.—CALCULATED DAILY RATES OF LONGITUDINAL GROWTH OF FEMURS FOR TEN DAY INCREMENTS

Rate for any Period = $\frac{\text{Distance for period}}{\text{Time of that period}}$			
Days	Min./Day	Days	Min./Day
20	.06	150	.04
30	.36	170	.05
30	.46	180	.06
40	.16	190	.06
50	.29	200	.06
60	.27	210	.06
70		220	.06
80		230	.06
90	.05	240	.06
00	.09	250	.06
10	.06	260	.06
20	.09	270	.06
30	.12	280	.06
40	.06	290	.06
50	.06	300	.06

Intervals from 10 to 300 days showed that the daily rates of growth decelerated with age in crease (Table III, Fig. 6). These measurements closely coincided with similar data on longitudinal growth of the femur as shown by Donaldson.

**Microscopic Measurements** which were made between the last two alizarine red S effects for specific age groups (Table I) showed that the increase at either the distal or the proximal ends alone was not equivalent to the total increase over-all for the femur at any given period. The sum, however, of the vertical increases at the distal and proximal ends closely coincided with the total increase over all (Table II, Fig. 5).

**Rates** The daily rates of growth, both experimental and calculated as shown by the alizarine red S effects decelerated with age increase. The latter assessments of daily rates (sum of distal plus proximal) closely coincided with the calculated rates which were obtained from the curve on measurements of length over-all (Table II, Fig. 5).

**Gradients** From the plotting of the decelerating rates on semilogarithmic graph paper (Fig. 6) it is evident that a gradient of growth

exists in the longitudinal growth of the rat femur. Logarithmic plotting of the total increments (Fig 7) resulted in a straight line graph and also makes it evident that a gradient of growth exists (Huxley)

**Subperiosteal growth** Measurements between injection effects in cross sections below the lesser trochanter showed that the distance between any two red lines was the amount of bone deposited for the given period at that level. The rates of growth were seen to be greater on the anterior than on the posterior surface (Table IV, Fig 8). The growth of bone beneath the periosteum also decelerated with age increase for anterior and posterior surfaces (Table IV, Fig 8).

**Statistical evaluation** on the basis of 1,034 trial measurements. The standard deviation was found to be 0.990 with a mean error of  $\pm 0.249$ .

#### ANALYSIS OF STUDY

**Pattern of growth** Textbooks of histology and embryology (1, 6, 15) have, to the present time, described the longitudinal growth of bone to take place by apposition at the diaphyseal side of the epiphyseal plate in the form of lines parallel to the epiphyseal plate. Our findings show the longitudinal apposition to be on the endosteal surface in the form of a cone whose base is the epiphyseal plate (Fig 4, A). Multiple injections of alizarine red S

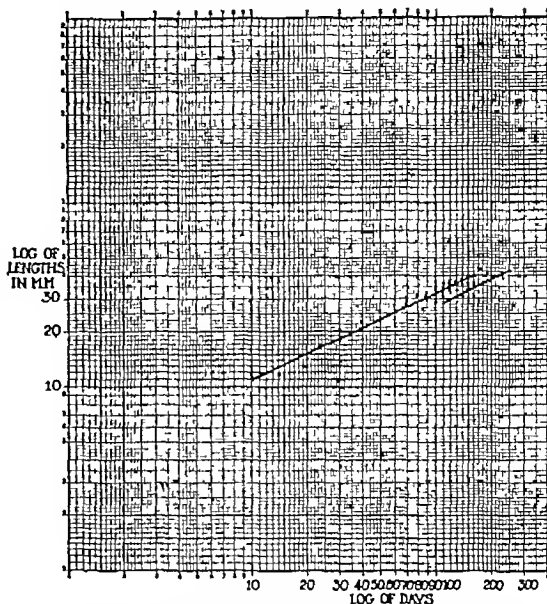


Fig 7 Graph showing the logarithmic plotting of the increments of longitudinal growth in the femur of 52 albino rats from 11 to 304 days of age

have demonstrated that the appositional process results in a series of cones, each succeeding injection effect dovetailed within the previous. From a three dimensional aspect, it can be demonstrated that each successive endosteal deposit at the base (epiphyseal plate) possesses a greater perimeter than the previous one, and

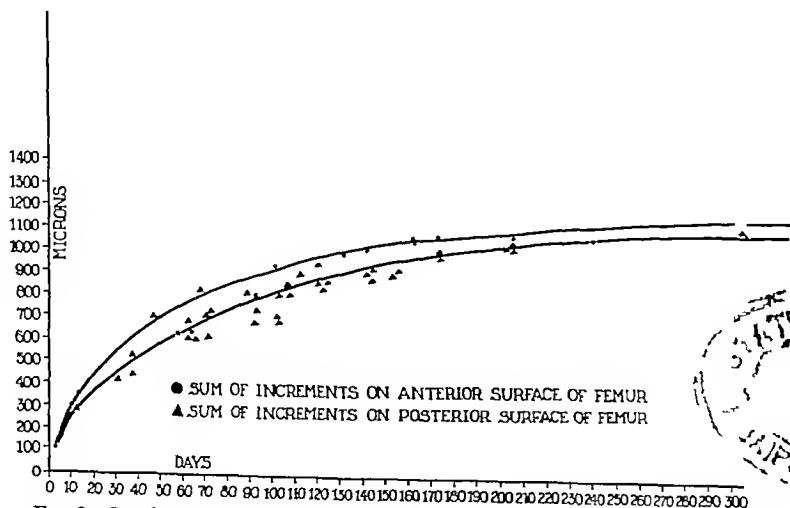


Fig 8 Graph showing calculated daily rates of periosteal growth at the anterior and posterior surface of the femur just below the lesser trochanter in 52 albino rats.

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No. of rat	Age in days	Growth at distal end in mm.	Growth at prox. end in mm.	Length of femur in mm.	Age (in days)	Total length in mm.
			0.4			36
17	46		0.0	0.6		36
30		3.7	0.0	3.9		
		0.0	0.0	3.9		3.4
104			1.1	3.4	61	66.38
17	6	0.0	0.1	3.4	61	67.84
06	8.4	1.84	1.1	3.4	61	68.57
106	8.4	6	7.5			66.66
	61	0.0	3.0	3.4	61	69.70
104	71	0.7	0.9	3.4	61	69.80
028	7	0.0	0.6	6	1.4	30.36
123	90	1.06	3.0	3.9		33.60
30	90	0.0	3.0	3.9	71	33.36
106	101	0.0	1.4	3.2	6	3.4
06	101	1	0.0	3.6		34.70
30	81	3.0	4.0	3.9	71	33.60
		0.0	0.0	3.9	71	33.90
10		7.5		3.2	90	33.70
100		1.7	0.5	0.9	71	33.78
100	90		4.5		90	33.76
13					90	33.37
09		2.3			90	33.80
09	3	3.3	0.7	0.8		31.60
100	30	1.3			90	31.60
	33	0.7	0.6			31.7
00	130	0.0			00	34.33
	1.1	0.1		3.2	130	34
003	141				90	36.77
	14	0.0	0.7	3.2	130	31.90
1.4			7.5	3.2	130	33.37
16	17	0.0	0.0	3.4	61	37.00
	17	0.0	0.0	3.2	130	37.00
		0.0	0.0	3.2	130	36.70
13	101	0.6	3.1	3.5		36.06
	006		3.0		71	36.00
09	206	0.5	0.0	3.6	007	36.70
00	206	1	3.3	3.6	003	37.00
06	51		0.0	3.7	003	38
79	201	0.13	0.4	3.7	003	37

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Rate for any Period = $\frac{\text{Distance for period}}{\text{Time of that period}}$			
Days	M /Day	Day	Mm /Day
10	0.6	100	0.6
00	3.6	170	0.1
30	3.6	0.0	0.6
40	1.6	100	0.7
50	0.9	000	0.5
60	0.7	130	0.6
70		00	0.5
80		30	0.6
90	0.6	130	0.0
100	0.9	130	0.3
00	0.9	160	0.0
130	0.9	170	0.0
30		0.0	0.6
130	0.6	100	0.6
70	0.6	300	0.0

Intervals from 10 to 300 days showed that the daily rates of growth decelerated with age increase (Table III Fig 6). These measurements closely coincided with similar data on longitudinal growth of the femur as shown by Donaldson.

**Microscopic Measurements** which were made between the last two alizarine red S effects for specific age groups (Table I) showed that the increase at either the distal or the proximal ends alone was not equivalent to the total increase over-all for the femur at any given period. The sum however of the vertical increases at the distal and proximal ends closely coincided with the total increase over all (Table II Fig 5).

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**Pattern of growth.** Textbooks of histology and embryology (1, 6, 15) have, to the present time, described the longitudinal growth of bone to take place by apposition at the diaphyseal side of the epiphyseal plate in the form of lines parallel to the epiphyseal plate. Our findings show the longitudinal apposition to be on the endosteal surface in the form of a cone whose base is the epiphyseal plate (Fig 4, A). Multiple injections of alizarine red S

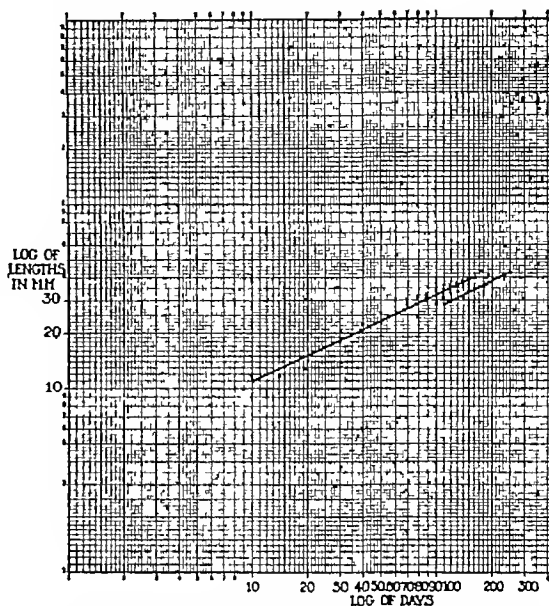


Fig 7 Graph showing the logarithmic plotting of the increments of longitudinal growth in the femur of 52 albino rats from 11 to 304 days of age

have demonstrated that the appositional process results in a series of cones, each succeeding injection effect dovetailed within the previous. From a three dimensional aspect, it can be demonstrated that each successive endosteal deposit at the base (epiphyseal plate) possesses a greater perimeter than the previous one, and

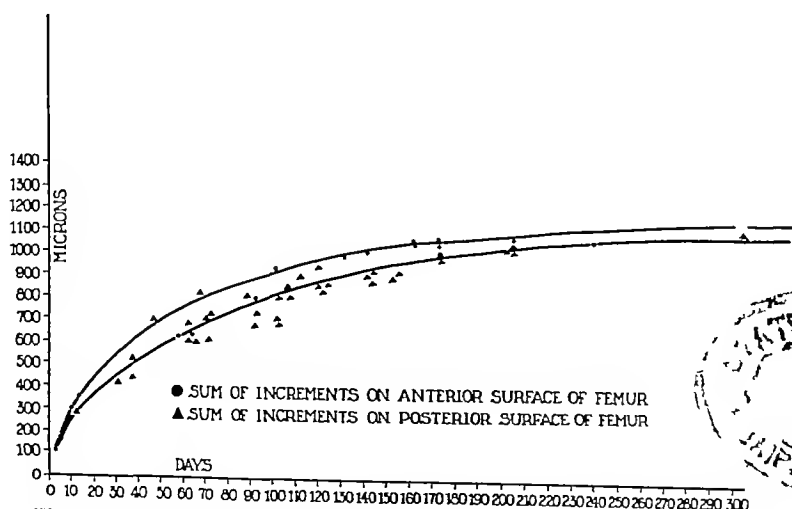


Fig 8 Graph showing calculated daily rates of periosteal growth at the anterior and posterior surface of the femur just below the lesser trochanter in 52 albino rats.

TABLE IV — CALCULATED DAILY RATES OF PERIOSTEAL GROWTH AT ANTERIOR AND POSTERIOR SURFACE OF FEMUR JUST BELOW LESSER TROCHANTER IN 52 ALBINO RATS

Age Interval	Anterior		Posterior	
	Amount of growth in microns	Increase per day in microns	Amount of growth in microns	Increase per day in microns
10-20	30		30	
20-30	130		80	8
30-40	200	20	70	
40-50	90		60	8
50-60	60	8	35	7
60-70	40	5	45	4
70-80	30	20	30	5
80-90	25	20	35	
90-100	25	20	35	
100-120	20	60	40	
120-130	20	40	30	
130-140	54	80	25	
140-150	15	60	20	
150-170	30	20	25	
170-180	75	60	20	
180-190	15	50		8
190-200	5	75		5
200-220	24	45		8
220-240	15	80		
240-270		60	80	
270-290		30		
290-320	8	54	8	
320-340		70	8	
340-370		75		
370-400	6	60		
400-470	8	60	6	6
470-500		55		
500-520		30		
520-550	5	30	5	5

consequently produces a flare at the epiphyseal line. The latter accounts for the increasing flare at the epiphyseal end of the bone with advance in age. As a result there is a tubularization pattern in the growth of the long bones.

The growth of the periosteal bone would, off hand, appear to limit the pattern of bone to a straight cylinder with parallel walls. However the periosteal growth follows the pattern of the internal cone and serves to increase the

width of the cortex with increase in age. Preliminary assessments of periosteal growth on the same material have shown that the rate of growth is greater in the region of the shaft near the subtrochanteric area than at the diaphysis. Hence, approximately the total diameter of the bone at the epiphyseal line is due to the flare of the legs of the cone within the diaphysis (Fig. 4). This morphological pattern which is found at the distal end of the femur is also seen in the neck, though quantitatively to a lesser degree in the latter. The endosteal arrangement in cones as found in the femur was also found in the other long bones.

**Mechanics of growth pattern.** The structural growing pattern of the femur consists of two series of truncated cones with bases facing away from the shaft at both ends. The tibia at its proximal end presents a pattern similar to and approximately a mirror image of the growth pattern of the distal end of the femur.

Hence, on either side of the knee joint there is a series of truncated cones whose bases are separated only by the epiphysis of the femur and tibia, respectively. Weight is transmitted from the shaft of the femur to its wide distal base and received by the corresponding cup at the proximal end of the tibia.

Such an arrangement is one of the strongest geometric configurations known to engineering for weight support and serves for balanced equilibrium in force distribution. Columns with a cap and base are commonly employed by architects to support buildings.

**Model.** It was necessary to construct a transparent model of the femur to clarify in our minds the three dimensional effects of alizarine red S. The model was prepared by compressing a mixture of the monomer and polymer of methyl methacrylate (Lucite) in a negative stone mold encased in a steel flask.

**Lines of arrested growth.** The peripheral base of each cone explains the so called Harris "lines of arrested growth" (10). Harris has described these lines seen on x-ray films. Brash has superposed serial x-ray films of Harries and has attempted to explain tubularization of bone on this basis. At present we are utilizing the alizarine red S method of vital injections to experimentally elucidate the significance of these "lines of arrested growth."

*Outlook* The method for study of normal bone growth as described in this investigation may be readily employed in experiments dealing with studies (1) involving growth stimulating or growth arresting substances, (2) healing of fractures, (3) bone grafting, and (4) the fate of grafts, and other problems related to normal and pathologic conditions in bone

# SUMMARY AND CONCLUSIONS

1 This study was based on the gross examination and microscopic study of the ground longitudinal and cross sections of the femurs of 52 albino rats, 10 to 305 days of age, which were given multiple intraperitoneal injections of a 2 per cent solution of alizarine red S (100 milligrams per kilogram) at specified intervals. Quantitative assessments were made of the rates of longitudinal and subperiosteal growth. The pattern of morphological growth was analyzed as a result of the alizarine red S effects

## 2 Findings show

a The longitudinal growth of long bones is a result of superposition of serial cones within the diaphyseal portion of the shaft, the bases of which cones are the epiphyseal plate at any given period

b The periosteum deposits bone on the circumferential surface of the shaft only and does not contribute toward the longitudinal growth of the femur

c The distal end of the femur grows faster than the proximal end (neck). The sum of the growth at both ends accounts for the total increase in length

d The longitudinal growth and the growth in width follows a growth gradient—the rates decelerating with increase in age

e Haversian system growth as shown by the alizarine red S effects occurs on the surfaces of the vascular canals. The red rings were seen to parallel the haversian lamellae. The diameter of the canals during appositional growth decreases with age

3 The morphological pattern of the tubularization of bone is compared to mechanical

supports as utilized in engineering and bears out the application of this mechanical arrangement to the knee joint

4 Suggestions are offered for further investigation on normal and pathological studies on bone, utilizing the vital injections of alizarine red S

# BIBLIOGRAPHY

- 1 AREA, L. B. *Developmental Anatomy* P 302 Philadelphia W B Saunders Co, 1930
- 2 BELCHER, JOHN. *Philos hist & mem Roy Acad Sc Par abr*, 1736, 39 287-299
- 3 BRASH, J. C. Some problems in growth and developmental mechanics of bone. *Edinburgh M J*, 1934, Pts 1-41, 305-387
- 4 CAMERON, G. R. The staining of calcium. *J Path & Bacteriol*, 1930-1932, 33 929
- 5 CHURCH. *Chemistry of Paints and Paintings* 4th ed., 1915
- 6 COWDRI, E. V. *Textbook of Histology* Philadelphia Lea & Febiger, 1938
- 7 DONALDSON, H. H. *The Rat* Wistar Institute of Anatomy and Biology P 190 Philadelphia, 1924
- 8 DUHAMEL, H. L. *Memoire sur la garance et sa culture etc Mém Acad roy d sc*, 1739-1741, 1742-1743, Paris, 1757
- 9 GRAEBE and LIEBERMAN. Quoted by Cameron
- 10 HARRIS, H. H. *Bone in Health and Disease* New York Oxford University Press, 1933
- 11 HERODOTUS. Quoted by Cameron
- 12 HOFFMAN, M. Personal communication
- 13 HOFFMAN, M. M., and SCHOUR, I. Rate and gradients of growth in rat molar as demonstrated by injections of alizarine red S. *J Dental Res*, 1938, 17 307-308
- 14 HUXLEY, J. S. *Problems of Relative Growth* New York Lincoln MacVeigh, Dial Press, Inc, 1932
- 15 JORDAN, H. E. *A Textbook of Histology* 5th ed P 72 New York D Appleton Century Co, 1930
- 16 KEITH, A. *Menders of the Maimed* Pp 222-264 New York Oxford University Press, 1919
- 17 KNECHT, RAWSON, and LOWENTHAL. *A Manual of Dyeing* 4th ed, 1917
- 18 PLINY. Quoted by Cameron
- 19 SCHOUR, I., and HOFFMAN, M. M. Daily rhythm in rat incisor demonstrated by injections of alizarine. *J Dental Res*, 1937, 16 349
- 20 Idem. Effect of alizarine red S injections on teeth and bones of Macacus rhesus monkey. *Proc Soc Exper Biol & Med*, 1938, 37 710-711
- 21 Idem. Studies in tooth development, No 2. The rate of apposition of enamel and dentine in man and other mammals. *J Dental Res*, 1939, 18 161-175
- 22 SCHOUR, I., SMITH, M. C., and HOFFMAN, M. M. Effect of vitamin A deficiency on rate of apposition of dentine. *Proc Soc Exper Biol & Med*, 1938, 39 447-450
- 23 WOOD, G. B. *Rubia tinctorum*. *Dispensatory of the United States of America*, 22nd ed Philadelphia J B Lippincott, 1937



# THE TENSILE STRENGTH OF SUTURED SKIN WOUNDS DURING HEALING

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THIS investigation was undertaken to study the healing of uncomplicated and complicated incised skin wounds in animals. In these experiments the degree of healing was measured by determining *in vivo* the tensile strength of the wound by the use of an apparatus which will be described later. Since the holding power of an incised wound, after the sutures have been removed, can depend upon little else than the degree of fibroplasia, the tensile strength should give an excellent index to the stage of healing. Uncomplicated incised wounds were observed to obtain a normal standard for this method of measurement. Wounds were opened and reclosed to obtain information on the value of secondary suture. Chronic catgut and silk were compared in another series of wounds, and the effect of avirulent bacteria as wound contaminants was studied. Finally observations were made upon the value of splenic extract and embryonic extract in the healing of incised wounds of the skin.

Howes, Sooy, and Harvey (6) were the first to study wound healing as reflected by wound tensile strength. They made wounds in the skin, fascia, muscle, and stomach of dogs. The animals were sacrificed at varying intervals; the wounds were excised and their tensile strength determined with a thread-testing machine. Later Harvey attacked the problem by making wounds in the stomach of the rat, and found the strength of the wound by inflating the viscus with air. In those experiments the workers demonstrated a standard curve for wound healing, which shows a quiescent period for the first 4 to 6 days, followed by a rapid gain in wound tensile strength until 10 to 14 days, when maximal wound strength is obtained. The latter stage is termed the phase of fibroplasia. It is of interest that Car-

rel had reached somewhat similar conclusions in his observations upon the diminishing surface area of open wounds.

## METHOD

A total of 77 adult guinea pigs and 11 adult dogs was used. The former were given all they could eat of a diet consisting of one-third whole bran, one-third cut hay and one-third bruised oats. Green cabbage and water were given in unlimited quantity. The dogs received a stock diet of meat and scraps, with water as desired. The diets contained adequate carbohydrate, fat, protein, and vitamins for the requirements of these animals.

All wounds were made under ether anesthesia after preparation of the shaven skin with ether and iodine. Aseptic operating room technique was rigidly adhered to and the wounds were dry before suturing. In the guinea pigs, two 3 centimeter wounds were made in each animal, one on each side of the spinal column approximately 1.5 centimeters from and parallel to it. Eight vertical 4 centimeter incisions were made on the abdomen of the dogs, distributed so that their blood supply was approximately the same. All wounds were through the skin and subcutaneous tissue only and were closed with a single layer of interrupted untreated 6/8 pound tensile strength, silk sutures. The silk was sterilized by autoclaving 5 minutes at 20 pounds pressure. At end of operation a dry sterile dressing was applied.

The wounds were tested on various days after operation. In each guinea pig both wounds were tested at the same time and two more wounds were tested on the same day in each dog. When the wounds were to be tested, the animals were anesthetized with ether and the dressing was removed. A Mikkel skin clip 3 millimeters wide, or a small towel clip was then firmly clipped into the skin on each side at right angles to the approximate midpoint on the wound and about 1 centi-

From the Wilkes Surgical Research Laboratory, University of Edinburgh, Scotland.  
George Corham Peters, Traveling Fellow in Surgery, Peter Bent Brigham Hospital, Boston, Massachusetts.

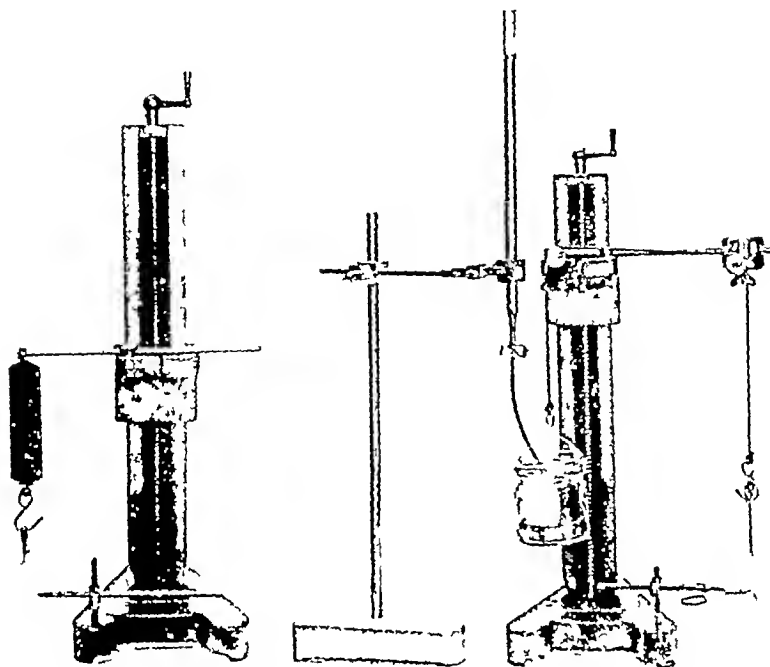


Fig 1 Tensiometer for opening skin wounds, with spring balance  
Fig 1a Tensiometer with pulley and mercury bucket

meter from it. The wound tensile strength testing apparatus pictured in Figure 1 was used. The hooks *A* and *B* (Fig 2) were inserted through the loops of the skin clips. The wound sutures were now gently removed. The screw handle *C* (Fig 2) was then slowly turned. This exerted constantly increasing tension upon the *A* side of the wound, whereas the *B* side remained fixed. The tension at which the wound gave was read directly from the spring balance *D* (Fig 2). For wounds over a tensile strength of 1000 grams, a cord, a pulley, and a small bucket were substituted for the spring balance (Fig 1a). Mercury was dropped into the bucket from a burette, and the total weight necessary to open the wound was easily calculated. When the test was finished, the wound was reclosed with sterile Michel skin clips. Infected wounds were not used except in the wound contaminant experiment. Whether this method of determining wound tensile strength *in vivo* is as accurate as that done with excised specimens is debatable. However, when wounds of similar size are tested in the same fashion each time,

the error should be constant and the results consistent and accurate for comparison in a series. A total of 252 wounds was thus tested.

#### RESULTS

*Group I* In this group the wounds were all uncomplicated, incised wounds sutured with fine silk. The curve of wound healing for 65 such wounds in guinea pigs is shown in Figure 3. The progress of healing, as measured by wound tensile strength, is slow but definite until the fourth day, thereafter there is a rapid rise in tensile strength until the tenth day, when the tensile strength remains more or less constant until the eighteenth day, which was the limit of the experiment. It is likely that in a given animal with 2 wounds made at the same time, the healing of the wounds should parallel each other, provided the blood supplies are equal and that infection is absent. In a series of 14 guinea pigs, each with two wounds, 8 of the animals had wounds that had tensile strengths within 100 grams of each other, while 6 showed a difference of 100 to 200 grams.

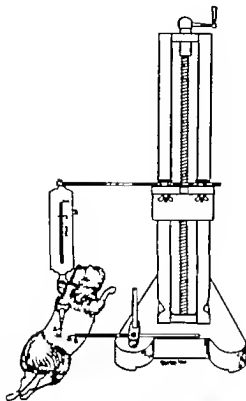


Fig. 2. Illustration of the use of the tensiometer

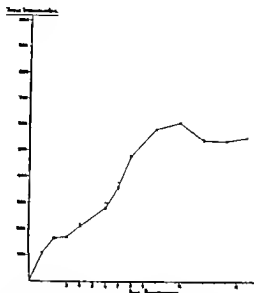


Fig. 3. Tensile strength of skin wounds in guinea pigs during healing. —, mean curve      ---, individual wound strengths.

As seen in Figure 3 the animals tested on any particular day showed considerable variation in the tensile strength of their wounds, and this variation tends to increase as the mean tensile strength becomes greater. Thus, on the eighteenth day the readings varied from 350 grams to 850 grams, the range being 500, while on the first day the range was only 221 (9 gm. to 240 gm.) It might be anticipated that the range would be approximately proportional to the mean, and for this reason the coefficient of variation was calculated; this is the standard deviation  $S$  divided by the mean  $M$ . As the number of animals tested on any particular day was few the standard deviation was computed for

each day by the formula  $S = \sqrt{\frac{\sum (V_i - M)^2}{n-1}}$

where  $V_i$  represents the separate readings  $V_1, V_2, \dots, V_n$  and  $n$  equals the number of readings. The average value of the coefficient

of variation so calculated was found to be 0.71. An estimate was also made of the coefficient of variation for multiple wounds in single guinea pigs from animals that had two wounds each. The average value was 0.24. This is much less than that found for wounds in different animals, and it suggests that in guinea pigs, individuals show considerable differences with regard to wound healing which are much in excess of those shown by a single animal.

The curve for healing in 27 incised skin wounds in dogs is shown in Figure 4. The curve is of special interest for it is very similar to that reported by Howes, Sooy and Harry from the determination of the strength of excised skin wounds in dogs. The gain in tensile strength is relatively slow until about the sixth day when there is a rapid rise until the eighth day and then a gradual gain in strength until the sixteenth day. Eight wounds in a single dog were tested in pairs at 4-day intervals for 16 days. None of the wounds was infected, and grossly they appeared much the same; however the differences in the strengths of the wounds were striking (Table I). At each test, except the 4-day test, there was a difference in tensile strength ranging from 544 grams to 884 grams.

# BOTSFORD TENSILE STRENGTH OF SUTURED SKIN WOUNDS

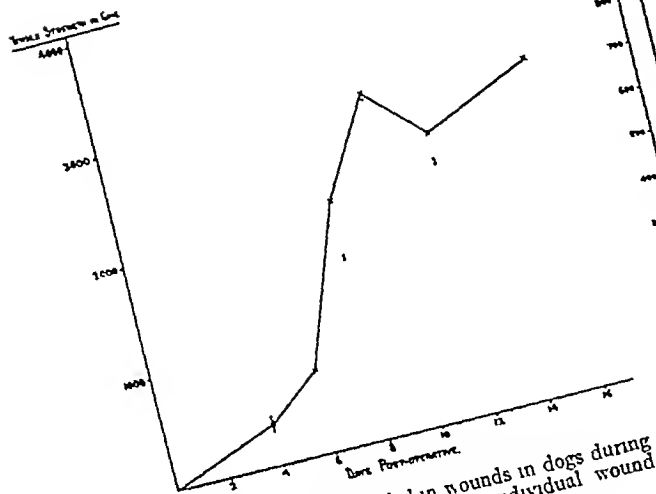


Fig 4 Tensile strength of skin wounds in dogs during healing strengths  
x—x, mean curve,  
—, individual wound

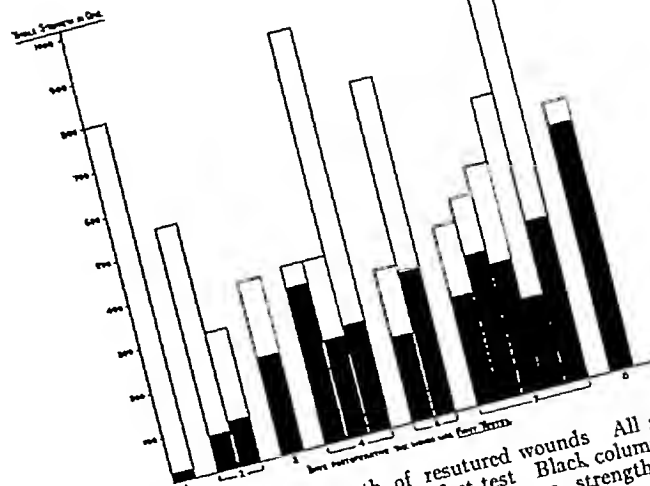


Fig 5 Tensile strength of resutured wounds. All re-tests performed 7 days after the first test. Black columns, original strength of wound, white columns, strength of second test.

The variability in a single dog is of much the same order as in a single guinea pig, but differs from animal to animal. The coefficient of variation for wounds in a single animal calculated from four pairs of wounds in one dog and was found to be 0.17. As this is derived from eight wounds, the standard error is considerably over 0.04 and does not differ significantly from the corresponding value of 0.24 found for guinea pigs. The coefficient of variation for different dogs was calculated to be 0.22, which is much less than the value for guinea pigs of 0.71. This means that the relative variation of tensile strength of wounds in dogs is only about one-third that found in wounds in guinea pigs. It is to be remembered that the actual strength of wounds in dogs is about five times that of guinea pigs, so that the range of tensile strength in grams is actually greater in the dog. It is, however, the relative strength that is important from a practical point of view and this is brought out by the coefficient of variation.

It is obvious that in interpreting the results of any study of wound healing, this variation in the healing of multiple incised wounds in single animals and from one animal to another must be considered. It also follows that wound healing varies with species.

A number of wounds in guinea pigs, reclosed after the original wound test, were retested 7 days after the secondary closure of the wounds. The gains in wound strength over the original strength after secondary wound closure are shown in Figure 5. This demonstrates that resutured wounds are stronger. In only two wounds (not shown on the chart) were the tensile strengths less than the original, both of these wounds infected. The increase in tensile strength in these secondarily closed wounds is great deal, and did not bear any relation to the original strength of the

TABLE I — VARIATION OF TENSILE STRENGTH IN MULTIPLE WOUNDS OF A SINGLE

Post operative day of wound test	No of wounds in dog	Tensile strength of wound in grams	Difference in grams	Coefficient of variation
4	1	350	50	2
	2	400		
	3	256		
8	4	1600	686	23
	5	3143		
12	6	2259	884	11
	7	3006		
16	8	1550	544	

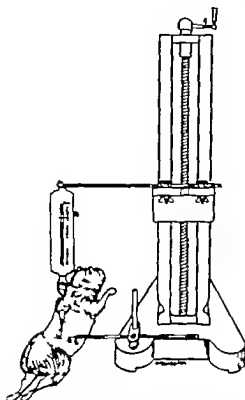


Fig. 2. Illustration of the use of the tensiometer

As seen in Figure 3 the animals tested on any particular day showed considerable variation in the tensile strength of their wounds, this variation tends to increase as the tensile strength becomes greater. Thus, on the eighteenth day the readings varied from 350 grams to 850 grams, the range being while on the first day the range was only 19 gm. to 240 gm. It might be anticipated that the range would be approximately proportional to the mean, and for this reason the coefficient of variation was calculated; this is the standard deviation  $S$  divided by the mean  $M$ . As the number of animals on any particular day was small, the standard deviation was computed for

$$S = \sqrt{\frac{\sum (x - M)^2}{n - 1}}$$

where  $x$  are the separate readings,  $M$  is the mean, and  $n$  equals the number of animals. The average value of the coefficient

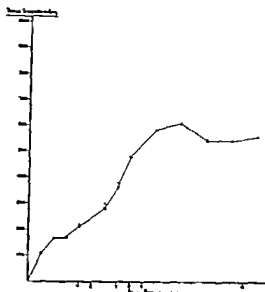


Fig. 3. Tensile strength of skin wounds in guinea pigs during healing. —, mean curve; x, individual wound strengths.

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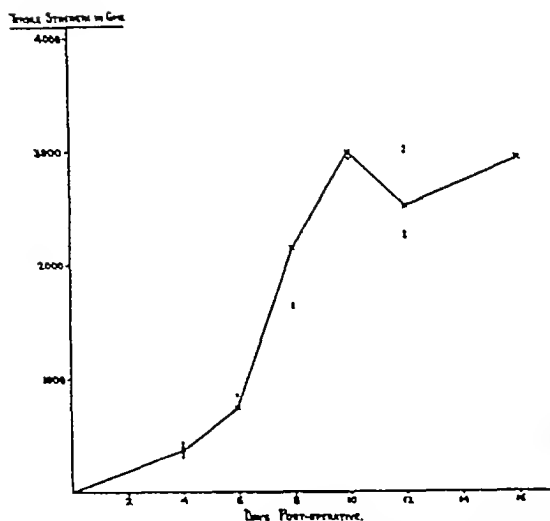


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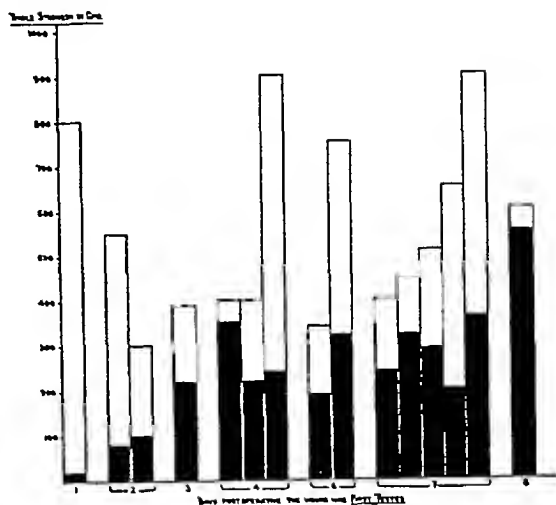


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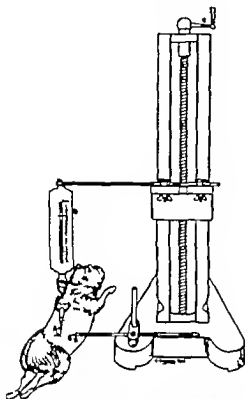


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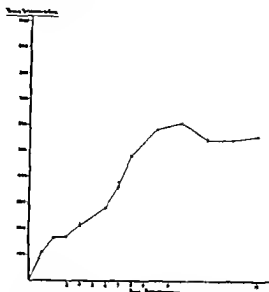


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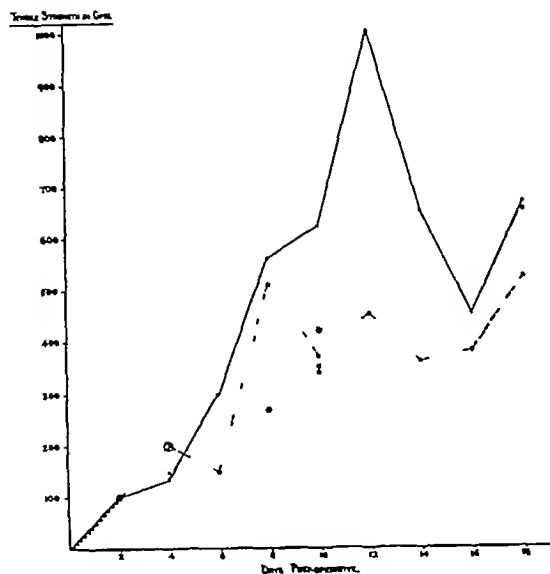


Fig 8 Tensile strength of skin wounds in guinea pigs, sutured with silk and with catgut. —, silk mean, o—o, catgut mean.

wounds sutured with catgut and silk, respectively, are real. This is further supported by the fact that of the 11 animals examined from the fourth day onward, everyone agreed, in that the wound closed with silk was superior in strength to that sutured with catgut. Assuming equal chances of catgut or silk appearing superior in any animal, the chance of the whole 11 agreeing is  $1/2^{10}$  or approximately 1 in 1000. The conclusion would seem justified that, after 4 days, skin wounds sutured with silk were less easily ruptured than those sutured with catgut in guinea pigs.

With regard to the fourth day (Fig 8), the observations are limited to 2 animals, but in both of these the catgut wound was stronger than the silk wound. Further examination of the figures suggests that this result is in fact a significant one, but it is inadvisable to be dogmatic in view of the small number of animals.

**Group IV** Recent reports by Nielson and Waugh have indicated that an embryonic extract developed by Dr Albert Fisher, of the Carlsberg Biological Institute, Copenhagen, is of value in accelerating the healing of open surface wounds both in man and in experimental animals. These workers measured the diminishing area of the open wounds, and, by

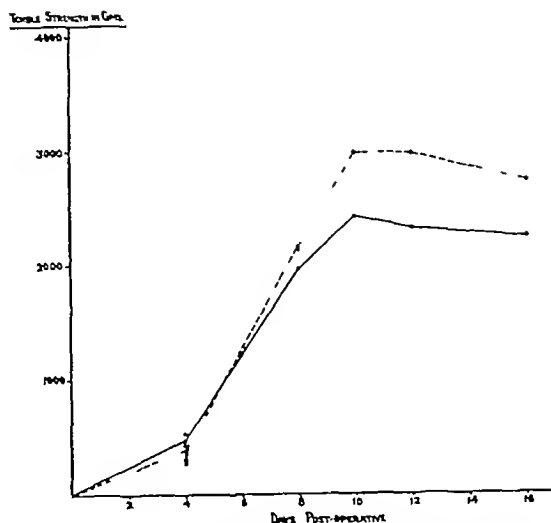


Fig 9 Tensile strength of skin wounds in dogs, treated with epicutan. —, mean of wounds treated with epicutan, o—o, mean of control wounds, oo, individual wound strengths

using du Noy's mathematical equation by which the rate of healing might be expressed and its normal course predicted, concluded that the preparation accelerated the healing by about 30 per cent. The preparation<sup>1</sup> of embryonic extract referred to is known as "epicutan" and is a protein derivative of embryonic tissue absorbed in kaolin powder (8).

Because of the foregoing work, it was thought to be of interest to determine the effect of epicutan upon wound tensile strength. Accordingly, the preparation was dusted into 12 wounds in dogs. There was one control wound for each treated wound. When the results are considered in Figure 9, it is at once apparent that epicutan has no appreciable effect upon wound tensile strength. The preparation is recommended for open surface wounds, and it might be said that this is not a fair trial.

**Group V** An extract of animal spleen was prepared by Dr J N Davidson, physiology department, University College, Dundee. This splenic extract was applied to wounds in guinea pigs and dogs to determine whether it had any effect upon the acceleration of wound healing.

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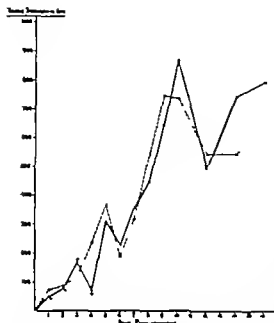


Fig. 6. Tensile strength of skin wounds in guinea pigs, contaminated with *Staphylococcus albus*. — wounds inoculated *o-o*, control wounds, + posth. culture from wound.

It is worth noting that the strongest wounds in the guinea pigs were in this group of wounds retested seven days after being opened.

**Group II** Because of the interest in causes of postoperative wound complications, the effect of avirulent bacteria as wound contaminants was studied. While these organisms usually do not cause wound suppuration, it was desired to find out if they have any effect upon the wound tensile strength. One wound in each of 13 guinea pigs was heavily inoculated with a 48 hour old dextrose broth culture of *Staphylococcus albus*, and in 8 guinea pigs a similar culture of *Bacillus subtilis* was used. These organisms were cultivated from room air. There was one control wound in each animal. Cultures were taken before operation from the skin and again from each wound as it was opened by the tensiometer. In 5 instances the pre-operative skin culture was positive for *Staphylococcus aureus*. Only one wound in this group became infected and that was a control wound. A mixed culture of *Staphylococcus aureus* and *Bacillus proteus* was obtained. In both groups of guinea pigs,

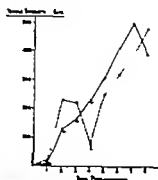


Fig. 7. Tensile strength of skin wounds in guinea pigs, contaminated with *Bacillus subtilis*. — wounds associated with *Bacillus subtilis*, *o-o*, control; + posth. culture from wound, I, infected control wound.

the contaminant was recovered by culture from the inoculated wound on every day from the first to the fourth day thereafter no organisms could be obtained by culture. In both the experiments the inoculated wounds were slightly stronger than the control wounds, although there was not much to choose between the control and contaminated wounds (Figs. 6 and 7). It would appear that mild wound infection has a favorable effect upon wound tensile strength. It is of interest to note the low tensile strength of the infected control wound (Fig. 7).

**Group III** In a series of 14 guinea pigs, one wound was sutured with two interrupted, No. 00 (Brit. Pharm.) 20 day chromic catgut sutures, while another wound in each animal was closed with two interrupted fine silk sutures. When the results given in Figure 8 are compared it is suggested that the catgut is slightly superior to the silk for the first 4 days but inferior on subsequent days. In the light of the great variability of wound healing in normal wounds, it would seem desirable to examine the figures from a statistical point of view. By use of the coefficient of variation (0.24) for two wounds in 1 animal an estimate was made of the standard error of the differences of the two wounds in each animal, and from this the probability *P* was obtained that the differences greater and equal to the observed ones should have occurred by chance. The value, *P* however was found to be less than 1/50 which confirms the conclusion that the differences between the

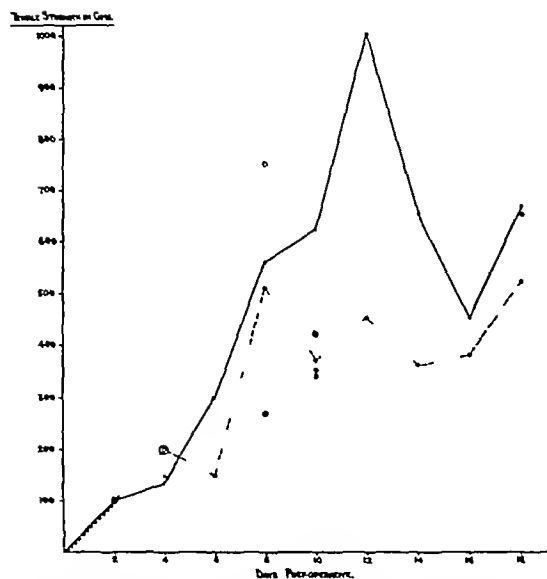


Fig 8 Tensile strength of skin wounds in guinea pigs, sutured with silk and with catgut. —, silk mean, o—o, catgut mean.

wounds sutured with catgut and silk, respectively, are real. This is further supported by the fact that of the 11 animals examined from the fourth day onward, everyone agreed, in that the wound closed with silk was superior in strength to that sutured with catgut. Assuming equal chances of catgut or silk appearing superior in any animal, the chance of the whole 11 agreeing is  $\frac{1}{2^{10}}$  or approximately 1 in 1000. The conclusion would seem justified that, after 4 days, skin wounds sutured with silk were less easily ruptured than those sutured with catgut in guinea pigs.

With regard to the fourth day (Fig 8), the observations are limited to 2 animals, but in both of these the catgut wound was stronger than the silk wound. Further examination of the figures suggests that this result is in fact a significant one, but it is inadvisable to be dogmatic in view of the small number of animals.

**Group IV** Recent reports by Nielson and Waugh have indicated that an embryonic extract developed by Dr. Albert Fisher, of the Carlsberg Biological Institute, Copenhagen, is of value in accelerating the healing of open surface wounds both in man and in experimental animals. These workers measured the diminishing area of the open wounds, and, by

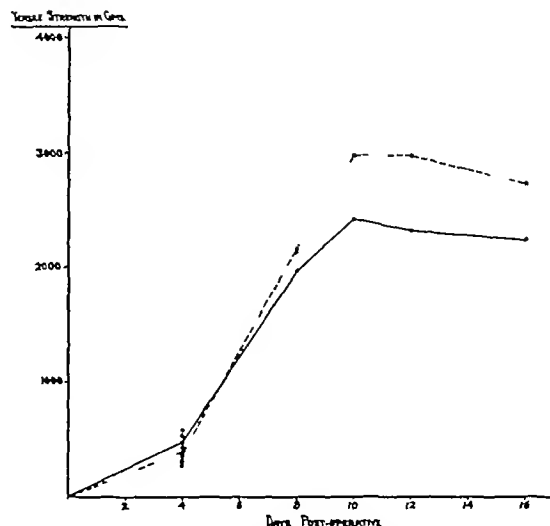


Fig 9 Tensile strength of skin wounds in dogs, treated with epicutan. —, mean of wounds treated with epicutan, o—o, mean of control wounds, oo, individual wound strengths.

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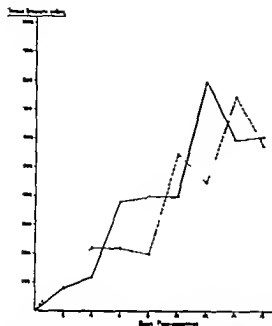


Fig. 9. Tensile strength of skin wounds in guinea pigs, treated with splenic extract — wounds treated with splenic extract o—o, control wounds

A consideration of the results from wounds in 8 guinea pigs (Fig. 10) shows that there was little difference between the treated and the untreated wounds, except that the splenic extract treated wounds did reveal a tendency for a gain in tensile strength to be more rapid than in the control wounds. The treated wounds in dogs, however did show a difference from the untreated wounds (Fig. 11). In 2 instances the control wound was stronger than the extract treated wound, while in 8 instances the reverse was true. When one performs a statistical analysis of these figures one finds that this figure (8 out of 10) cannot be regarded as very significant. The same conclusion is arrived at by the use of the coefficient of variation to calculate the expected variation by pairs and compare those with the differences actually observed. There is about one chance in twenty five of differences equal or greater than the observed arising. We may conclude that the experiments in the case of the dog wounds suggest that the application of splenic extract promotes wound healing as measured by the tensile strength of the wounds, but further work is required to prove that fact.

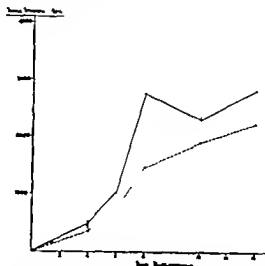


Fig. 10. Tensile strength of skin wounds in dogs, treated with splenic extract. — wounds treated with splenic extract, o—o, control wounds oo, individual wound strengths.

#### ANALYSIS OF STUDY

There is little indication for generalizations on experiments such as the foregoing for they have to be evaluated on their face value and it is also to be remembered that they are on animals and not on man. It is, however of interest to point out again the important factor of variation in healing in individual animals, and in animals with multiple wounds. This is knowledge that is of paramount importance in any study of wound healing. The factor of variation should hold true for open wounds as well as for incised wounds.

The gain in tensile strength of secondarily closed wounds coincides with the clinical experience of many (4) that disrupted wounds heal remarkably well if the patient survives. The fact that the contaminated wounds did well and the organisms disappeared rapidly is not salve for the surgeon's conscience but merely another indication of nature's ability to protect.

Catgut versus silk has long been a subject of dispute between the advocates of each. Here silk was shown to be superior to catgut as a skin suture in guinea pigs. The actual tensile strength of the suture material did not enter as the sutures were removed before the wounds were tested. The reaction of the tissues to cat

gut, which has been demonstrated by others (3) to be greater than that to silk, must be the underlying cause for the superiority of silk. This reaction, which is an exudative one, presumably delayed the onset of fibroplasia in these wounds.

The question of substances that may accelerate the healing of wounds is of perennial interest to the surgeon. The embryonic extract epicutan produced negative results as judged by the tensile strengths of the wounds concerned, but the trial of splenic extract in dogs was very suggestive of a beneficial action upon wound healing. This was not true in guinea pigs. Whether it is wise to attempt to accelerate the healing of incised wounds is a debatable point. In view of the variation in the healing of wounds in animals, an unstable factor in each individual, which is the inherent ability to repair damaged tissue, is more important than substances which accelerate wound healing when applied locally. This does not intend to imply that local treatment of wounds is not essential, but means that nature should be helped but not pushed. This conception is based upon observations on incised wounds, and it would not be wise to apply it to open surface wounds. Additional work on this subject will be necessary in order to clarify the problem.

# SUMMARY

- 1 A method for testing the tensile strength of wounds in animals *in vivo* is reported.
- 2 Normal curves of wound healing, as measured by the wound tensile strength of skin wounds *in vivo* in guinea pigs and dogs, are demonstrated.

- 3 The variation of the ability to heal among single animals and in the individual animal with multiple wounds is shown.
- 4 Experiments showing the value of secondary suture are described.

5 The superiority of silk over catgut as a skin suture is demonstrated.

6 Embryonic extract epicutan was found to have no effect, good or bad, upon wound healing as measured by wound tensile strength in dogs.

7 Splenic extract was found to be of questionable benefit in the acceleration of wound healing as measured by wound tensile strength in dogs.

I wish to record my thanks to Professor J. R. Learmonth for his advice and guidance in carrying out this work, and to acknowledge my indebtedness to the technical staff of the Wilkie Surgical Research Laboratory for their help. I also am indebted to Dr. W. O. Kermack of the Royal College of Physicians' Laboratory, Edinburgh, for his aid in the statistical analysis.

# BIBLIOGRAPHY

- 1 CARREL, ALEXIS. The treatment of wounds. *J. Am. M. Ass.*, 1910, 55, 2148.
- 2 DU NOÛY, P. L. General equation for the law of cicatrization of surface wounds. *J. Exper. Med.*, 1919, 29, 329.
- 3 HALSTED, W. S. The employment of fine silk in preference to catgut and the advantages of transfusing tissues and vessels in controlling hemorrhage. *Surgical Papers, The Johns Hopkins Press*, 1924, 1, 29-46.
- 4 HARTZELL, J. B., and WENFIELD, J. M. Disruption of abdominal wounds. *Internat. Abst. Surg.*, 1939, 68, 585.
- 5 HARVEY, S. C. The velocity of the growth of fibroblasts in the healing wound. *Arch. Surg.*, 1920, 18, 1227.
- 6 HOWES, E. L., SOOY, J. W., and HARVEY, S. C. The healing of wounds as determined by their tensile strength. *J. Am. M. Ass.*, 1929, 92, 42-45.
- 7 NIELSON, E. The influence of animal growth substance upon the course of wound healing. *Ugesk. f. Læger*, 1939, 37, 1071.
- 8 WAUGH, W. G. Experiments in the acceleration of wound healing. *Brit. M. J.*, 1940, Feb. 17, No. 4128, 249.

## MALIGNANT LESIONS OF THE CECUM AND ASCENDING COLON

CHARLES W. MAYO, M.D. F.A.C.S. and W. RANDOLPH LOVELACE, II, M.D.  
Rochester, Minnesota

**R**ESECTION of the right half of the colon including the cecum is the surgical procedure of choice in a variety of pathological conditions which affect this particular segment of the intestine. The most common of these is a malignant lesion.

The basis for this study is a series of 885 cases of malignant lesions of the cecum and ascending colon in which operation was performed at the Mayo Clinic in the years 1907 to 1938 inclusive.<sup>1</sup> These constitute about 80 per cent of all the malignant lesions of the cecum and ascending colon seen in this period. Cases in which the lesion was situated in the hepatic flexure of the colon were included but not those in which the lesion was distal to the hepatic flexure. In 358 or 40 per cent, of the cases the lesion was situated in the cecum and in 527 or 60 per cent it was situated in the ascending colon including the hepatic flexure.

In 295 of the 885 cases or 33 per cent, the operative procedures performed were not curative in purpose they included, for instance, exploration and biopsy, palliative ileocolostomy, cecostomy, and ileostomy. Also included in this group are a few cases in which palliative resection was performed in the presence of extensive metastatic involvement of the lymph nodes or liver.

In 590 or 67 per cent, of the 885 cases, resection was performed with a view to cure. This is worthy of note because nonpalliative resection is attempted in only about 50 per cent of cases of malignant lesions of the left half of the colon in which surgical treatment is employed. In 247 of the 590 cases the lesion was situated in the cecum and in 343 cases it was in the ascending colon.

From the Division of Surgery, the Mayo Clinic. Read before the meeting of the Western Surgical Association, Los Angeles, California, December 3 and 10, 1939.

The statistical calculations included in this study were made under the auspices of the Division of Biometry and Medical Statistics of the Mayo Clinic.

The percentage of surgical cases of malignant lesions of the cecum and ascending colon in which nonpalliative resection could be attempted has remained rather constant in the 32 years covered by this study although in the past 5 years there has been about a 3 per cent increase in the cases in which this was possible. This may be accounted for not only by earlier diagnosis but also by improvements in auxiliary surgical technique.

In order to determine the relative frequency of malignant lesions of the cecum and ascending colon and of other segments of the large intestine, we studied the histories of all cases in which operation for malignant lesions of the large intestine, including the anal canal, was performed at the clinic in the years 1907 to 1938, inclusive. The cases in which the lesion involved the cecum or ascending colon comprised 30 per cent of the cases in which the involvement was proximal to the termination of the sigmoid and 12 per cent of the entire group of cases.

This review is based on the summation of the operative experience of a rather large group of different surgeons. However the group was thought to be sufficiently homogeneous to permit us to make a detailed statistical study of certain aspects of the problem.

### AGE AND SEX

In this series of cases the age incidence was somewhat similar to that of carcinoma situated elsewhere in the body (Table I). In 20, or 2.3 per cent, of the 885 cases the patients were less than 30 years of age. In 14 of the 20 cases the lesion was in the cecum.

The impression of the surgeon that carcinoma which affects young people is more malignant than that which affects old people was supported by the results of a calculation of the 5 year survival rate. For the patients less than 40 years, the 5 year survival rate was

54 per cent and for the older patients it was 58 per cent. Deaths from all causes are included for these calculations. Since older people have a general death rate higher than younger people, correction should be made for the higher rates of the older people from other causes than cancer, if the true contrast so far as cancer is concerned is to be seen. When these survival rates were corrected for the normal death rates from causes other than cancer in the respective age groups, the 5 year survival rate for patients less than 40 years, exclusive of deaths from other causes than cancer, was found to be 55 per cent, and that for the patients 40 years or more of age was 66 per cent. This indicates a greater virulence of malignancy among the younger group.

#### RELATION OF MORTALITY RATE TO THE SURGICAL PROCEDURE

The gross hospital mortality rate for the entire series of 885 cases was 23.5 per cent. These cases include those in which only a palliative procedure was carried out as well as those in which it was possible to carry out resection with the object of cure. All deaths in the hospital are included, regardless of the cause of death or the time that had elapsed since operation.

In general, which is safer, a one stage or a two stage resection of the cecum and ascending colon? Most surgeons consider a two stage operation the safer procedure from the standpoint of operative mortality, and statistics from various hospitals and clinics seem to bear this out. Ransom recently reported a mortality rate of 32 per cent for one stage resection, in contrast to a mortality rate of 20 per cent for two stage operations. Allen (1, 2) reported a mortality rate of 20.5 per cent for one stage resection in 73 cases of carcinoma of the right portion of the colon and a mortality of 11 per cent in 18 cases in which a two stage procedure was performed.

Pemberton and Whittaker reported a series of 46 consecutive cases, in 8 of which single stage procedures were performed and in 38 of which two stage procedures were performed. In addition to the 46 cases, there were also 5 cases in which ileocolostomy was performed as the first part of a two stage operation. In the

TABLE I — AGE AND SEX OF PATIENTS TREATED SURGICALLY DURING 1907 TO 1938, INCLUSIVE

Age years	Lesion in cecum		Lesions in ascending colon	
	Patients	Per cent	Patients	Per cent
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10-19	5	1.4	0	
20-29	8	2.2	6	1.1
30-39	33	9.2	54	10.2
40-49	69	19.3	101	19.2
50-59	117	32.7	151	28.7
60-69	99	27.7	173	32.8
70+	26	7.3	42	8.0
Total	358	100	527	100
Youngest patient	6 years		23 years	
Oldest patient	79 years		84 years	
Mean age	53.7 yrs		55.2 yrs	
Males	218	60.9	330	62.6
Females	140	39.1	197	37.4

38 cases in which the two stage resection was performed there were 2 deaths, a mortality rate of 5.2 per cent, there were 2 deaths in the 5 cases in which ileocolostomy only was performed as the first of a two stage procedure. In the total group of 43 cases in which two stage resection was contemplated, the mortality was 9.3 per cent. In the 8 cases in which a single stage operation was performed, there was 1 death. With good reason, Pemberton is an advocate of the two stage method of resection of the right half of the colon.

Harvey, however, advocated the one stage procedure and, in 1934, reported 18 cases of carcinoma of the cecum in which operation was performed with a mortality of 11 per cent. Stone and McLanahan (1939) advocated a one stage procedure whenever possible and also an aseptic type of end-to-end anastomosis. Jones advocated the use of an end-to-side anastomosis when a one stage resection is carried out. Lahey advocated a modified Mikulicz procedure with staggering of the proximal portion of the ileum for removal of malignant lesions in the right portion of the colon. He said that this type of operation obviated the danger of leakage and peritoneal contamination.

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One of the most important advantages of one stage as compared to the two stage resection of the colon in cases of neoplasm in our opinion concerns the factor of time. It is reasonable to suppose that the longer a malignant lesion remains in the body the greater is the risk of extensive metastasis which will preclude resection.

One of us (C. W. M.) has performed one stage resection of the right portion of the colon in an all inclusive series of 49 cases up to and including 1939, with a hospital mortality rate figured regardless of time or cause of 12.2 per cent. In the same period of time, a two stage resection was performed in 8 cases in this group 1 death occurred after completion of the second stage of the operation and 3 deaths occurred following an ileotransverse colostomy. In fairness to the two stage resection however it must be stated that in the cases selected for this type of operation the condition was more serious, an important point to be kept in mind.

Until the present report, no large series of cases of malignant lesions of the cecum and ascending colon has been presented for comparison as to operative procedures and results. Of course, a review of such a large series as is included in the present report is made possible only by including the experience of several surgeons who have differed among themselves as to the advantages of different types of operations. It does not take into account the advantages of improved pre-operative and post operative care characteristic of recent years. In the 590 cases in which operations were carried out with a view to cure, there were 315 in which a one stage resection was performed, 246 in which a two stage procedure was utilized and 29 in which more than a two stage procedure was employed. A review of the hospital mortality for this entire group would seem to indicate that the one stage resection has an advantage over the two stage procedure as the one stage resection resulted in a hospital mortality of 22.2 per cent as compared with a hospital mortality rate of 28.9 per cent for the two stage procedure, 15 per cent after the first stage and 13.9 per cent after the second stage. In the group of 29 cases in which resection was performed in

more than two stages, there were 10 deaths in the hospital.

No case in which death has occurred in the hospital has been eliminated regardless of how long after the operation it occurred or the cause of death. There is no intention in presenting the general mortality figures to depreciate any individual surgical method because it is evident that the individual surgeon may master a method and obtain results which will justify the method in spite of what may appear to be a condemnation in the general picture.

In considering the hospital mortality rate for one stage operations from the viewpoint of type of anastomosis, it was found that the hospital mortality rate was 22.7 per cent in cases in which a side to-side anastomosis was done, 23.4 per cent in cases in which an end to-side anastomosis was performed, and 19.2 per cent in cases in which an end to-end anastomosis was done. Because of the technical difficulties, it is often impossible to carry out an end to-end anastomosis, but it apparently is the procedure of choice when it can be accomplished. Comparison of the 5 year survival rates for the one stage and two stage types of resection showed a small advantage in favor of the one stage type after 5 years even with the hospital mortality disregarded. The 5 year survival rate in cases in which the one stage procedure was used was 57.8 per cent as compared with 55.3 per cent for the two stage. Although the difference is small and must be viewed as tentative until an even larger series of cases can establish the survival rates, it is interesting that in this total series of cases the one stage operation is advantageous both so far as the immediate hospital mortality is concerned and also so far as the 5 year survival of those who withstood the operation successfully is concerned.

A review of the hospital mortality according to the age of the patient confirmed the general impression that mortality is very definitely greater as the age of the patient increases. While the hospital mortality for the whole group of patients who were subjected to operation with a view to cure was 25.6 per cent, that for the individuals less than 40 years of age was only 14.7 per cent, that for

individuals between 40 and 60 years was 21.0 per cent, while the mortality rate for individuals more than 60 years of age was above the average rate and increasingly so for individuals more than 70 years of age. In cases in which the value for the hemoglobin was less than 7 grams per 100 cubic centimeters of blood the mortality rate was 36.8 per cent, in cases in which the value was between 7 and 12 grams the mortality rate was 28.1 per cent, and in cases in which the value was more than 12 grams the rate was 22.3 per cent. Similarly, in cases in which the erythrocyte count was less than 3.5 million per cubic millimeter of blood the mortality rate was 39.5 per cent, as contrasted with a mortality of 16.7 per cent in cases in which the erythrocyte count was more than 4.5 million. In 97 patients in whom there was a perforating lesion, the mortality rate was 29.9 per cent, this as contrasted with a mortality rate of 24.7 per cent in those patients in whom perforation had not taken place.

#### MORBIDITY ASSOCIATED WITH ONE STAGE AND TWO STAGE RESECTION

In cases in which a one stage operation was performed 49 per cent of the patients spent a total time of less than 20 days in the hospital and 43 per cent spent between 20 and 35 days, the average was 21 days. In cases in which a two stage resection was performed, 22 per cent spent a total of between 20 and 35 days in the hospital and the rest spent more than 35 days in the hospital, the average was 45 days. Only 8 per cent of patients subjected to a one stage resection were in the hospital more than 35 days, 78 per cent of those who underwent a two stage procedure spent this length of time in the hospital. In addition, one must also consider the fact that in more than half of the cases in which the two stage procedure is used the patients must spend time, sometimes a considerable period, in the hospital between the first and second stages of the operative procedure. In the cases in which a two stage resection was performed, 13 per cent of the patients were out of the hospital for 20 to 34 days between the stages and 13 per cent were out of the hospital for 35 days or more.

#### THE QUESTION OF ILEOSTOMY

It often has been stated that an ileac stoma made proximal to the site of anastomosis acts as a safety valve which prevents distention of the intestine with gas and fluid and thus tends to prevent leakage and subsequent peritonitis. Our study indicates that ileostomy is an added hazard which increases the operative mortality. Ileostomy was performed in 98 cases. In all of these cases the Witzel method was used. The mortality rate in the 98 cases was 6 per cent higher than it was in the cases in which enterostomy was not performed. Ransom found that the increase in the mortality rate in cases in which ileostomy is performed usually is due to general peritonitis or severe infection at the site of the incision, which often results in a persistent fecal fistula. He concluded that performing an enterostomy is not only unnecessary but unwise. Our findings have led us to the same conclusion.

#### ONE STAGE RESECTION

In the majority of cases in which resection of the colon has been performed for malignant lesions of the cecum and ascending colon by one of us (C W M), a one stage procedure has been employed and an end-to-side ileo-transverse colostomy has been performed.

#### PROGNOSIS AND FURTHER STATISTICAL ANALYSIS

At present the most satisfactory method of determining prognosis in the individual case of malignant lesion of the colon, rectosigmoid, rectum, and anus is the combined application of Broders' method of grading of malignancy, which is based on the dedifferentiation of cells, and Dukes' (4, 5) classification of such neoplastic growth, which is based on the mural penetration of malignant cells.

Simpson and one of us (C W M), in 1939, reported on the effect of mural penetration of carcinoma cells in the colon. The work was based on an examination of 120 carcinomas of the colon. Dukes' (4, 5) method of classification was modified to fit growths situated above the rectosigmoid and at the same time the growths were classified according to Broders' method of grading. It was concluded that the deeper the carcinomatous penetration, the

TABLE II.—GRADE OF MALIGNANCY

Site of involvement	Cases*	Per cent of cases			
		Grade 1	Grade 2	Grade 3	Grade 4
Cecum	206	14	37.8	33	15
Ascending colon	277	9.4	34	47.2	9

\*Only cases in which grade of malignancy was determined are included.

greater was the probability of involvement of lymph nodes and the greater was the probability that the growth would be of a histological grade of malignancy. Likewise, the higher the histological grade of malignancy the deeper is mural penetration likely to be found, and the more likely it is that lymph nodes will be involved. However these factors were found to operate independently to a certain degree in that for any class of penetration the prognosis is poorer the higher the histological grade of malignancy similarly for any histological grade of malignancy the deeper the penetration the worse the prognosis. The most precise prognosis is obtained if Dukes (4) method of classification of mural penetration is combined with Broders histological grading of malignancy.

Does the situation of the lesion have any influence on the grade of malignancy? If so what is the status of the cecum and right half of the colon in such a consideration? In both the cecum and the ascending colon one of the most typical features of malignant lesions is the high percentage of tumors which have a low grade of malignancy. While tumors which have a high grade of malignancy do occur and in a percentage greater than in the left portion of the colon, rectosigmoid, rectum, and anus, analysis of the cases in which Broders scheme of grading was used (Table II) shows that 65.6 per cent of the carcinomas in the cecum and 64.2 per cent of the tumors in the ascending colon were grade 1 or 2. Classification of these tumors by Dukes system would in all likelihood be of additional value, but an insufficient number of neoplasms in this present series of cases were classified by this method to warrant analysis.

Does the grade (according to Broders classification) have any influence on the percent age of cases in which metastatic involvement

TABLE III.—GRADE OF MALIGNANCY AND METASTASIS TO LYMPH NODES

Grade	Cases*	Cases with nodal metastasis	
		Number	Per cent
1	5		20
2	7		29
3	60		51.7
4	14	3	21.2

\*Only cases in which grade of malignancy was determined are included.

of lymph nodes is present? Metastatic involvement of lymph nodes was noted in 28 per cent of the total number of cases in this series. It was present in 31 per cent of the cases in which the lesion involved the cecum and in 26 per cent of the cases in which the lesion involved the ascending colon. This percentage of metastasis is higher than it is for the rest of the large intestine. In those cases in which the grade of malignancy was determined histologically there was a progressive increase in the incidence of involvement of lymph nodes as one passes to the higher grades of malignancy (Table III). The lymph nodes were involved in only 22 per cent of the cases in which the lesion was grade 1 whereas they were involved in 59 per cent of the cases in which the lesions were grade 4. This brings out the correlation between the degree of malignancy as it is determined by histological examination and as it is manifested by metastatic involvement. Metastasis to the liver was noted by the surgeon in only 10 per cent of the cases.

It has been noted that when spread of a malignant growth begins through lymphatic channels, the nearest lymph nodes are usually the first to be involved. Neither such involvement of lymph nodes adjacent to the tumor nor even involvement of lymph nodes deep in the mesentery of the right colon should preclude resection of the malignant lesion.

In a recent review of the lymphatic distribution of the colon and rectum Looney stated that there are comparatively few lymph nodes along the ascending colon and those that are present lie along the medial margin. The lymphatic vessels of the appendix, cecum, ascending colon, hepatic flexure and the right

TABLE IV—SURVIVAL RATES IN CASES IN WHICH OPERATION WAS PERFORMED WITH A VIEW TO CURE

Period after leaving hospital	Patients who survived operation*		Survived beyond indicated period	
	Total	Traced	Number	Per cent of traced patients
5 years	302	298	170	57.0
10 years	225	219	104	47.5
15 years	155	150	56	37.3
20 years	91	88	22	25.0

## FIVE YEAR SURVIVAL RATES

	Patients who survived operation*		Lived 5 or more years after leaving hospital	
	Total	Traced	Number	Per cent of traced patients
Cecum	127	125	67	53.6
Ascending colon	175	173	103	59.5
Total	302	298	170	57.0

\*Inquiry as of January 1, 1939. The 5 year group comprises the patients operated on 5 years or more prior to the time of inquiry, that is, 1933 or earlier; the 10 year group comprises those operated on in 1928 or earlier and so forth.

two-thirds of the transverse colon follow, in general, the distribution of the superior mesenteric artery and end in the superior mesenteric lymph nodes whence the lymph passes through the gastro-intestinal trunk to the cisterna chyli. Raiford stated that the lymph supply to the cecum and right half of the colon is not abundant because this portion of the bowel is primarily concerned with the absorption of fluid. Despite these facts, it has been the observation of one of us (C. W. M.) that the lymph nodes of the right portion of the colon are efficient in maintaining within themselves metastatic deposits for a long period without permitting more distant spread.

## SURVIVAL RATES

A word is in order about the way in which the calculation of survival rates was made. For each survival rate, the patients who were operated on the requisite number of years prior to the time of inquiry (which was as of January 1, 1939) were first selected. That is, for the 5 year survival rate the patients operated on in 1933 or earlier were selected, for the

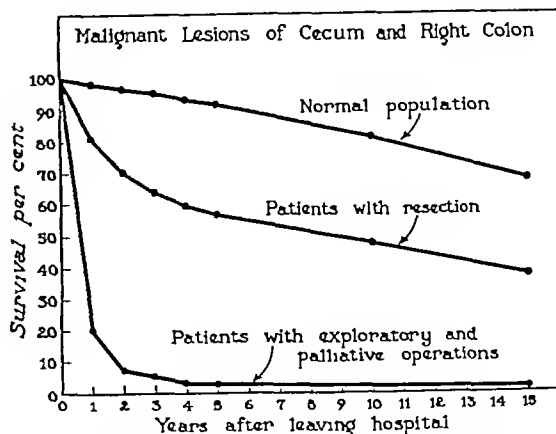


Fig. 1. Survival rate in cases in which resection was performed with a view to cure.

10 year rate, those operated on in 1928 or earlier were selected and so forth. Obviously, therefore, the 5 year rate was calculated on the basis of a larger number of patients than the 10 year rate, the 10 year rate on a larger number of patients than the 15 year rate. Only the patients traced for the requisite number of years were included in the calculation. For instance, of the patients operated on 10 or more years before the date of inquiry, that is, in 1928, or earlier, only those who were traced for 10 or more years were utilized in the calculation of the survival rate. Hence, a patient who had been operated on 10 years prior to the time of inquiry but traced for only 6 years after operation and living at that time was included as traced for the 5 year calculation but was considered untraced for the 10 year calculation.

An exhaustive effort was made to trace all patients. When patients were delinquent in answering the routine follow-up letter, the local health departments, vital statistics bureaus, and so forth, were consulted to learn whether any record of death existed. In the end, only a small fraction of the patients remained untraced. More than 99 per cent of the patients who were operated on 5 years or more before this investigation were traced for 5 years or more.

The survival percentages were calculated on the basis of the patients who withstood the operation successfully, that is, operative mor-

TABLE V.—FIVE YEAR SURVIVAL RATES ACCORDING TO GRADE OF MALIGNANCY—OPERATION PERFORMED WITH VIEW TO CURE

Grade	Total number of patients traced	Per cent of survival
1	22	77.4
2	25	82.6
3	28	57
4	22	4.5

tality was not included in the calculation of survival rates. Here, as elsewhere in this study operative mortality includes all deaths which occurred in the hospital regardless of cause of death or length of time in the hospital after operation.

Table IV presents the survival rates of the patients on whom resection was performed with the purpose of cure, and Figure 1 shows the survival curves for this group compared with that for the patients who underwent palliative operations and with that for the normal population. One of the most striking and encouraging results of this study is the finding of a survival rate exclusive of hospital mortality of 57 per cent at the end of 5 years for the group in which resection was performed. It is remarkable that 22 of the 88 patients, or 25 per cent, were alive at the end of 20 years. Further study of the 22 patients who survived 20 years or more shows that 10 patients have survived 25 years or more. On examination of the lesions of these patients 2 were not graded 2 were grade 1 3 were grade 2 2 were grade 3 and 1 was grade 4. In 1 case in which the lesion was grade 2 the patient is alive 31 years after resection, and in another case in which the grade of malignancy was not determined the patient is alive 30 years after resection.

Comparison of the 5 year survival rates and the site of involvement (Table IV) reveals that 53.6 per cent of the patients were alive at the end of 5 years in the group with lesions in the cecum in contrast to a survival rate of 59.5 per cent when the lesion was situated in the ascending colon. One might hazard the explanation that there is a tendency for the surgeon not to be radical enough in cases in which

TABLE VI.—FIVE YEAR SURVIVAL RATES ACCORDING TO INVOLVEMENT OF LYMPH NODES AND GRADE OF MALIGNANCY OPERATION PERFORMED WITH A VIEW TO CURE

Group	Patients who purpose of operation*		Living 20 years after leaving hospital	
	Total	Traced	Patients	Per cent of traced patients
Local involvement Grade 1 and 2		22	21	95
Grade 3 and 4			15	40
Not graded	72	72		40
Total	72	172	36	47
No local involvement Grade 1 and 2	197	197		70
Grade 3 and 4	20	20		30
Not graded	20	27		43
Total	237	244		64

\*See footnote to Table IV.

the neoplasm is limited to the cecum considering the fact, as has been shown, that in cases in which the lesion is in the cecum the incidence of metastatic involvement of the lymph nodes is higher than in cases in which the lesion involves the ascending colon.

A study of survival rates in relation to Broders histological method of grading of neoplasms confirms its prognostic value. The lower the grade of malignancy the greater are the relative number of patients alive at the end of 5 years. Table V shows how definite is the relationship between the grade of malignancy and the ultimate results. Of 31 traced patients with grade 1 lesions, 77.4 per cent were alive at the end of 5 years, whereas only 42.3 per cent of those whose tumor was grade 4 survived 5 years. It is clear that the grade of malignancy is an outstanding factor in determining results since the survival rate decreases progressively as one passes to the higher grades of malignancy.

The prognostic importance of involvement of the lymph nodes in addition to grade in respect to the 5 year survival rate is shown in Table VI. In cases in which involvement of the lymph nodes was associated with lesions which were grade 1 or 2 56.4 per cent of the traced patients were alive at the end of 5 years. In cases in which the grade of malignancy

nancy was the same but there was no involvement of the lymph nodes, 70.1 per cent of the traced patients were alive at the end of 5 years. Of the patients who had grade 3 or 4 lesions which were associated with involvement of the lymph nodes, 40.0 per cent of those who were traced survived for 5 years. In cases in which lesions grade 3 or 4 were not associated with involvement of the lymph nodes, 59.0 per cent of the patients who were traced were alive at the end of 5 years. Regardless of the grade of the malignant lesion, the chances are less in cases in which the lymph nodes are involved than they are in cases in which there is no involvement of the lymph nodes. This table also brings out that, given the fact of the presence or absence of involvement of lymph nodes, the higher the grade of the lesion, the lower will be the number of patients who are alive at the end of 5 years. It should also be noted that although the presence of involvement of the lymph nodes justifies a guarded prognosis, absence of this finding does not necessarily rule out regional extension or metastasis.

#### SUMMARY

This paper is based on a statistical study of 885 cases of malignant lesions of the cecum and ascending colon, including the hepatic flexure, in which surgical treatment was employed. The study is accumulative for the entire group of these cases which were seen at the Mayo Clinic in the years 1907 to 1938, inclusive. The results presented represent a summation of the work of a considerable number of different surgeons. It must be remembered, therefore, that this presentation is not based on the experience of an individual surgeon nor is it based only on the work as it is done today. For any particular type of operative procedure, whether it be performed in a single stage or in multiple stages, the individual statistics from the standpoint of mortality or morbidity may be better or worse than the general average disclosed by this study.

The main findings are as follows: malignant lesions of the cecum and ascending colon (including the hepatic flexure) constitute 30 per cent of malignant lesions of the abdominal colon, and 12 per cent of malignant lesions of

the entire colon including the rectosigmoid, rectum, and anal canal. In 62 per cent of the cases the patients were males and in 38 per cent they were females. In 80 per cent of cases in which the lesion involved the cecum or ascending colon the patients were between 40 and 70 years of age. The average age was 55 years. Anemia is not only an important diagnostic consideration but also definitely increases the operative risk.

Resection with a view to cure was performed in 67 per cent of the cases in this series. This percentage is higher than that reported in cases in which the lesion was found elsewhere in the large intestine. There are many varieties of single stage and multiple stage procedures employed in resection of the cecum and ascending colon. In the interest of the patient, the surgeon should be familiar with all of these procedures. The net hospital mortality rate in all cases and from all causes was 23.5 per cent. Mortality, on the same basis, in cases in which resection was performed with a view to cure, that is, excluding exploration and palliative operations was as follows: for one stage resection, 22.2 per cent, for two stage resection, 28.9 per cent, and for more than two stage resection, 34.5 per cent. This would seem to indicate that, when a one stage resection is found possible and surgically advisable, it has an advantage, in respect to average mortality, over other methods. In 8 per cent of the cases in which a one stage resection was performed, the patients remained in the hospital for more than 35 days, whereas in 78 per cent of the cases in which a two stage procedure was performed, the patients remained in the hospital for 35 days. In cases in which the two stage procedure was employed, 13 per cent of the patients were out of the hospital for 20 to 34 days and another 13 per cent were out for 35 or more days between the two stages. The duration of the malignant lesion in the body appears to have some influence on the 5 year survival rate. In the cases in which the patients were traced the 5 year survival rate was 2.5 per cent greater in cases in which a one stage resection was performed than it was in cases in which a two stage procedure was employed. Enterostomy as an auxiliary surgical measure in any method of

resection of the right portion of the colon appears to be contraindicated as a 6 per cent increase in mortality was found in cases in which this procedure was employed. Survival rates were calculated for various groups in the series. In the group of cases in which resection was performed with a view to cure the survival rate for 5 years was 57 per cent for 10 years, 48 per cent for 15 years, 37 per cent and for 20 years 25 per cent.

Grading of neoplasms by the method of Broders has again been shown to be of prognostic value. The survival rate decreases progressively with the higher grades of malignancy. In 65 per cent of the cases the lesion was grade 1 or 2. Involvement of the lymph nodes has been shown to increase directly with the grade of malignancy and to be of prognostic value both independently and in association with the grade of the neoplasm. In cases in which the lesion was grade 1 or 2 and not associated with involvement of the lymph nodes, the 5 year survival rate was 70 per cent. In cases in which the lesion was grade 3 or 4 and associated with lymphatic involvement the 5 year survival rate was 40 per cent. The presence of lymphatic involvement need not be regarded as presenting a hopeless prognosis. In cases in which the lymph nodes were involved 47.2 per cent of the patients were alive 5 years or more after resection.

## REFERENCES

- ALLER, A. W. Right colectomy for malignant disease—discussion of mortality associated with various operative procedures. *J Am M. Ass.* 937 909-923-926.
1. ALLER, A. W. and WELCH, C. E. Malignant disease of the colon, factors influencing the operability, morbidity and mortality. *Am. J. Surg.* 1930, 48 77-180.
2. BRODERS, A. C. The grading of carcinoma. *Minnesota Med.*, 915 8 795-796.
3. DEWEY, C. E. The classification of cancer of the rectum. *J. Path. & Bacteriol.*, 932, 35 323-33.
4. Idem. Extension and classification of tumors of the rectum and of the colon. *Am. J. Surg.*, 1930, 40 181-185.
5. HARTY, S. C. The one-stage operation for resection of the cecum and proximal colon. *New England J Med.*, 934, 930-944.
6. JONES, T. E. The treatment of cancer of the colon. *Surg. Gynec. & Obst.* 935, 6 4 5-419.
7. LAMONT, F. H. Neoplasms of the cecum and ascending colon. *Am. J. Surg.* 1930, 40 5-7.
8. LOONEY, W. W. The lymphatic distribution of the colon and of the rectum. *Am. J. Surg.* 1930, 40 143-145.
9. PATE, NICOLAI. Cancer coll. *Acta chirurg. Scand.* 934, 74 457-462.
10. PENNINGTON, J. J. and WHITTAKER, L. D. Resection of the right half of the colon. *Surg. Gynec. & Obst.*, 937 65 93-99.
11. RAYBURN, T. S. Treatment of carcinomas of the large bowel. Part I. The colon. *Ann Surg.* 933, 804-825.
12. RAYBURN, T. S. Carcinoma of the right colon. *Surg.* 1930, 5 340-357.
13. SCHROEDER, W. C. and MAYO, C. W. The neural innervation of the carcinoma cell in the colon, anatomic and clinical study. *Surg. Gynec. & Obst.* 1930, 68 878-877.
14. STONE, H. B. and McCLAVARA, SAMUEL. Surgical aspects of carcinoma of the large bowel. *J Am M. Ass.* 1930, 3 2262-2268.





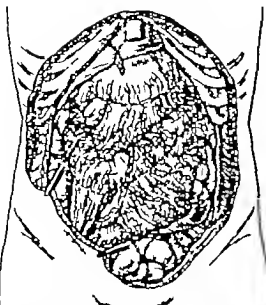


Fig. Post-operative omental adhesions. Fixation of the omentum to low abdominal incision, left right lateral and dorsum and displacement, and fixation under tension of the transverse colon. Fixation under tension is more important in causing dysfunction of the colon than is displacement alone.

from standing erect. She got some relief from bearing down, and from applying heat to her abdomen. This pain was associated with nausea and regurgitation of food into her mouth after every meal. She began to have reflex vomiting of liquids and foods, about months before the current admission. Constipation gradually increased during this whole period, until at the time of admission it had become intractable. Cathartics taken by mouth even in large quantities were of no avail, so that she came to lead an enema life. A large part of every morning was spent taking repeated enemas which entailed the greatest suffering because they irritated intense colics. Even with these repeated daily enemas she procured only one movement every 2 or 3 days. A bowel movement caused colic, but subsequently the defecation brought relief. As the constipation increased the colics became unbearable, and as the constipation became less severe the colics subsided somewhat. During the past 2 years this suffering was associated with unusual intermittent distention of the abdomen with borborygmi, which would develop rapidly and force her to let out her coiled strings several inches. By this time she was so incapacitated and invalidated that she could not carry on her duties as nurse. Exertion caused great discomfort, and the effort of walking up and down stairs initiated intense colics. She learned from experience that by limiting the intake of nourishment to liquids during the cyclically recurring spells of

colic, distention, obstipation and nausea, she could bring about subsidence of an attack when nothing else would avail. As roentgen studies showed the transverse colon fixed and angulated in the pelvis, operation was advised and accepted. This revealed an omentum adherent in the pelvis and lower abdomen. When the adhesions were released, the medial 8 inch segment of the mobilized transverse colon was seen to form an acutely angulated loop with the two limbs of the angulated loop adherent to each other over a stretch of 4 inches, from constrictures in the gastrocolic omentum. These constrictures were severed, and the limbs of the transverse colon separated so as to eliminate the acute angulation. The omentum was resected, and the gastrocolic omentum was reefed. The entire small bowel was absolutely free of adhesions. Exploration of the rest of the abdomen was negative. Postoperative roentgen studies (Fig. 2 Case 5) showed the transverse colon elevated from the pelvis, reduced in diameter with more normal haustrations. All angulation had disappeared. There was marked axial shortening of the transverse colon, a spontaneous change apparently due to restoration of muscle tone in the released bowel. Following operation there was immediate restoration of spontaneous daily bowel movements for the first time in years. On the tenth day the patient slipped from surveillance to try climbing stairs, and could do it without any discomfort. In 1 year she gained 5 pounds. For 3 years she has been completely free of all symptoms. There is no nausea, vomiting, or colic, and her bowels move daily with never any need for laxative or enema. The patient has been completely restored to normal health, and does a full day's work regularly.

In grouping the cases for study it is apparent that the initial symptoms appear from a few months to several years following an abdominal operation through a low abdominal incision. The syndrome was never encountered following operations through only a high abdominal incision. The symptoms group themselves into three types: first reflex symptoms; second, colon symptoms; and third, pentoneal symptoms. The reflex symptoms, developing early or late in the picture, are characterized by epigastric distress after eating with nausea, regurgitation, and later vomiting. These reflex symptoms occur immediately while eating or within a half hour also with attacks of colic. They last from a few minutes, to half an hour or more. Vomiting in the later periods may assume such serious proportions that no liquids or foods are tolerated by the patient with resultant malnutrition, exhaustion and serious dehydration.

If the reflex disturbance is late in developing, the second group, or colon symptoms—colicky pain, intractable constipation, distention, pain with enemas, painful bowel movements with relief after defecation—appear and dominate the picture. The colon distress consists of intermittent spells of sharp colicky pain, usually in the epigastrium, sometimes in the right or left hypochondrium or lower toward the pelvis. In the absence of extreme fixation of the colon, occasional mild discomfort as from crowding by gas, may announce the bowel involvement. The colicky pain tends to maintain a constant location in each patient, that point depending upon the type of involvement of the colon by adhesions. If there be true angulation of the bowel, as revealed by roentgen study, the colicky pain may be at that point. If the function of the colon is disturbed by tension exerting itself at either the hepatic or splenic flexures, the localization of pain coincides with the area of disturbed physiology—right or left hypochondrium—sometimes with radiation to the back. The location of the pain is predominantly epigastric and right upper quadrant. In the event of failure to procure complete relief by simple lysis of adhesions, the position of the pain may change, depending upon the anatomical relocation of the transverse colon. The onset of the colicky pain is related to eating, defecation, or use of an enema (gastrointestinal activity), also to exertion and abdominal trauma (peritoneal irritation). It comes on arising in the morning, later in the day, or during the night. As time passes it comes more frequently, several times a day, and its intensity augments. Coming in the morning it may be so intense that the patient is unable to move from the bed for half an hour or more, and is forced to lie doubled over, arms around the abdomen, bearing down for relief. There is considerable audible borborygmi during the spells. The patient frequently experiences pain on breathing while enduring these colics.

Constipation varies directly with the intensity of the colic. In the early periods there are less frequent bowel movements with a feeling of incomplete evacuation. As the pain becomes more acute and lasting, the constipa-

tion becomes intractable. Massive quantities of cathartics are taken with diminishing effectiveness, and the patient ultimately comes to lead an "enema life." Daily enemas sometimes procure a movement once or twice in several days. The use of an enema or a spontaneous bowel movement may precipitate sudden agonizing colic, although complete defecation subsequently brings relief. There is usually direct correlation between the intensity of the colic and the degree of constipation. As the constipation becomes more marked, the pain is intensified. As the constipation abates, the attacks of pain subside—but only to recur with aggravation of the constipation. In some cases the attacks last for several days, subside, and then recur at intervals of several weeks. In other cases there is constant suffering. In the later periods of severity, the reflex symptoms of nausea and vomiting are aggravated. Vomiting comes once to several times a day and finally occurs whenever liquid or food is taken by mouth. At the height of the crisis of colic and constipation, this constant vomiting produces an extreme loss of nourishment and body fluids. There results an excessive loss of weight with marked dehydration. Rarely is there ever vomiting of upper bowel contents (so called fecal vomiting). A large number of these cases noted that some relief from colic was obtained by going on liquid diet which eliminates the bulky fecal stream. This fact probably accounts for the confusing relief experienced on a liquid Sippy regimen. This fact often leads to the suspicion of an ulcer. One patient attained comfort by maintaining constant watery stools with large daily doses of epsom salts.

Distention is not experienced by all the patients, despite this unmanageable bowel function. The most critical stage of malnutrition, from the vomiting and constipation phases of the syndrome, may be reached without any distention. In most cases, however, distention occurs in varying degrees from intermittent increase of the girth by 2 or 3 inches, to the extreme sudden distention of an acute obstruction. Such an extreme distention is unusual, but may appear overnight. One patient awakened one morning with so marked a distention that a nurse remarked

she "looked nine months along." This distention responds temporarily to medical measures, but only to recur promptly. In mild cases it occurs chiefly after eating. In severe cases, after several days or weeks of distention with associated vomiting and complete obstipation the distention gradually abates, with progressive subsidence of the other symptoms. Recurring chronic colics then dominate the picture until the next acute seizure develops.

The third group of symptoms (peritoneal) are due to constant tension and intermittent traction on the colon via this fixed omentum, from the pull of physical effort. Some patients become conscious of an intra-abdominal pulling sensation. Colicky pains are stirred up in the colon by the traction that results from exertion. Some patients are caught suddenly with acute discomfort after starting to walk, so that they have to stop on the street and return home. Flexion and extension of the leg or bending the body sometimes initiates pain. One patient had the first sudden seizure of agonizing pain after the unusual exertion of playing twenty-seven holes of golf; another experienced the onset of colic after a severe fall which produced a tearing sensation within the abdomen. Still a third patient spent three-fourths of every day in bed to avoid the discomfort caused by the jouncing of an obese abdominal wall; other patients had to give up driving a car because of suffering entailed by the frequent extension of the foot on the pedals; a few patients were awakened from sleep at night by pain initiated from extension of a leg kept flexed to minimize their discomfort. Women stated that they had to give up scrubbing floors because of the intense colic resulting. Kneeling in church acted similarly. The support of a girdle sometimes relieves the downward traction on the omentum and reduces the discomfort. This peritoneal phase is probably augmented by a low grade inflammatory process and microscopic tears of the omentum, as evidenced by the round cell infiltration and hemorrhagic exudate seen in histological sections. Clinically this possibility is suggested by occasional fevers (99 to 102 degrees) and leucocytosis (6 cases 11,000 to 15,000).

On physical examination, downward traction of the abdominal wall by the palms of the hands placed over the incision sometimes evokes the characteristic pain. Abdominal tenderness is frequently elicited and is possibly related to a low grade epiploitis with regional irritation of the involved peritoneum.

When first seen by the physician these patients present one of three composite clinical pictures. First, and least common, there is an explosive onset of symptoms bearing the features of an acute abdominal emergency. The patient is taken suddenly with unendurable colicky pain, which causes him to cry aloud, and requires repeated injections of morphine for relief. Repetition of the colics, associated with unusual constipation and vomiting lasts for days. All symptoms gradually abate. This type of onset is associated with falls and with unusual exertion. The second group of patients complain characteristically of chronic colics. They give a jumbled story of nausea, vomiting, intermittent distention and constipation with persistently recurring colic, which, until carefully integrated, makes a confusing clinical picture. Acute exacerbations of these chronic symptoms may occur after a fall. Presumably tearing of the fibers of the adherent omentum augments the malfunction of the transverse colon and the related symptoms. This fact may well account for many baffling seizures of acute upper abdominal pain seen in patients with previous laparotomies, after a serious fall. The third clinical picture characteristic of the advanced stages of the lesion is that of recurring spells of apparent subacute intestinal obstruction. Frequently recurring intense colics are associated with marked persistent distention, cessation of bowel movements, nausea, and vomiting. This vomiting usually consists in immediate expulsion of slightly altered fluids and foods shortly after they are ingested. Very rarely there is vomiting of small bowel contents (fecal vomiting) but this suggests concomitant involvement of the small bowel by adhesions. Such obstructive seizures last for several days to weeks, gradually abate, and then are followed by the second type of clinical picture—chronic colic with constipation and occasional vomiting. Roentgen studies reveal

no evident cause for the clinically apparent obstruction. Too frequent recurrence of these critical seizures brings the patient to a state of extreme malnutrition and exhaustion, with death threatened by starvation and dehydration. One patient was observed for 1 year until her death from vomiting, debility, and inanition (Fig. 27).

#### PATHOLOGY

The post-operative fixation of an omentum to a low abdominal incision is usually a harmless occurrence. In occasional cases, however, an adherent omentum undergoes progressive fibrosis and shortening which produces deleterious results. Fibrosis is initiated at the point of fixation of the omentum and propagates itself in response to the stimulus of trauma, exertion, or infection. This progressive fibrosis replaces the fat and gives a firm consistency to the adherent segment of the omentum. The shriveling action of this fibrosis may shrivel this segment to a quarter or a sixth the length of the nonadherent portion of the organ. The extent of involvement of the omentum and colon by adhesions occurs in four degrees: first, adherence of a small area of omentum to the scar; second, adherence of a wide area with definite slight downward displacement of the transverse colon; third, marked contraction of a large fixed segment, pulling the colon deeply into the lower abdomen so as to underlie the incision; fourth, extensive surface involvement of the peritoneum with extension of the fibrosing process through the greater omentum up into the gastrocolic omentum, and associated with marked ptosis of the colon. The displacement of the colon is usually proportionate to the degree of involvement of the adherent omentum (Fig. 2).

Histopathological alterations parallel these gross modifications of the omentum. In contrast to the normal omentum (Fig. 3) with its homogeneous network of fat cells containing occasional small bundles of connective tissue, the early stages of this lesion reveal propagating fibrillar processes of connective tissue. These fibrils invade the fatty tissue (Fig. 4), insinuating themselves among the fat cells. The fat cells thus encroached upon become

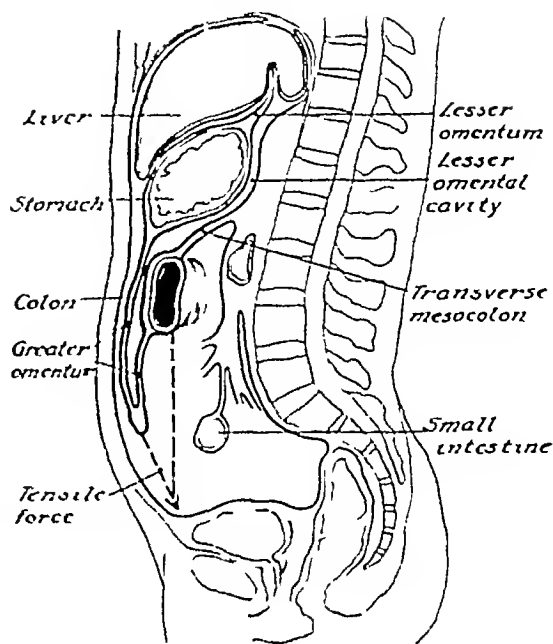


Fig. 2 Mechanism of displacement. Diagrammatic representation of the anatomic relations of transverse colon to the greater omentum, in the layers of which it is incorporated. A tensile force, which depresses the greater omentum, will simultaneously depress and immobilize the transverse colon. A fixed progressively fibrosing and contracting omentum will steadily depress the level of the transverse colon, thus subjecting it to increased tension, displacement, and fixation.

compressed, reduced in diameter, and sometimes obliterated. Coalescence of these fibrils yields heavy strands of connective tissue which propagate themselves in direct continuity. From these heavy strands, distinct peaked projections of connective tissue spread directly between adjacent fat cells, engulfing, isolating, and obliterating them (Fig. 5). Rarely, the stimulus of repeated operative trauma causes complete replacement of all the fat by a homogeneous sheet of connective tissue (Fig. 6). Detailed histological study reveals an obliteration of fat lobules by proliferating fibroblasts, with engulfment of the irritating end-products of disintegrating fat by numerous giant cells (Fig. 7). Granulating tissue appeared in the partially obliterated lobules of fat ahead of the fibrosing process. Active fibroblasts pervaded all the tissue. Scattered areas of hemorrhage and leucocytic infiltration depicted the influence of trauma.



Fig. 3.

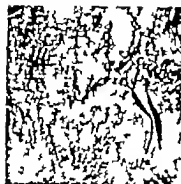


Fig. 6.

Fig. 3. Normal omentum, connective tissue bundle. The web-like appearance of sheet of fat cells constituting the normal omentum. At the left of the section note the single discrete bundle of connective tissue. To the right of this is a small zone of collagen or elastic-like fibrous material. Note the complete absence of invasive characteristics, there being no involvement of adjacent fat cells by extension of this connective tissue component into the normal fat tissue. To the right of the central point of the section are two very small discrete accumulations of lymphocytes and polymorphonuclear leukocytes.  $\times 30$ .

Fig. 4. Filaments of connective tissue. Left portion of section is composed of heavy condensed filaments of connective tissue which has engulfed many individual fat cells, obliterating them in the areas of heavy collagen deposit. From this heavy deposit fiber filaments insulate themselves to the right among the individual fat cells, gradually fading away between the normal fat cells in the right part of the section. Note the smaller compressed appearance of the fat cells in the central portion of the section. At the upper and lower borders of the section is evidence of hemorrhage, to which this process of organization may be related, and which indicates tears from physical exertion and falls.  $\times 30$ .



Fig. 4.



Fig. 5.



Fig. 7.

Fig. 5. Strands of connective tissue. Here  $\gamma$  strands of connective tissue are directly invading and obliterating the lobules of fat. From the edges of these strands peaked projections of connective tissue extend directly between adjacent fat cells. Discrete fat cells appear engulfed along the border of the strands. This is evidence of direct extension in continuity of this connective tissue strand, in dependence of propagation by fine fibrils as seen in the preceding section.  $\times 30$ .

Fig. 6. Sheet of connective tissue. Complete replacement of fat lobules by continuous sheet of connective tissue. In the upper portion of the section are three completely surrounded lobules, slowly undergoing disintegration from invasion and compression by the sheet of connective tissue. To the extreme right is seen the terminal stage of obliteration, with accumulation of giant cells.  $\times 30$ .

Fig. 7. Giant cell obliteration of fat lobule. High power study of fat lobule mentioned in the preceding section. Disintegrating fat establishes foreign body brilliant reaction, which calls forth this giant cell reaction. In the same area are large numbers of eosinophiles and young active fibroblasts, evidence of simultaneous destruction of fat, and up-building of connective tissue elements.  $\times 5$ .

This fibrotic shirring of the fixed omentum caused yielding and downward displacement of the incorporated portion of the transverse colon with its ultimate fixation. At exploration whereas the left transverse colon and

omentum hung freely in the upper abdomen the right transverse colon passed sharply downward across the abdomen toward the right lower quadrant. Here the colon was fixed, not directly itself but indirectly by fix



Fig 8 Case 1 Left, pre-operative, right, postoperative views Roentgenogram before operation showed dilatation, loss of haustrations, and single fixed loop of transverse colon, postoperative roentgenogram showed bowel with smaller lumen, normal haustra, and U shaped loop of colon Patient was a female, aged 26 years who had had an appendectomy at 14 years Immediately she had spells of colic requiring morphia Defecation occurred every 7 days Intermittent distention became the size of 9 months' pregnancy Vomiting occurred several times daily She was awakened at night by colics At operation fecal impaction was noted proximal to fixed loop The adherent omentum was released Complete relief of symptoms followed the operation and she since had daily bowel movements

ation of its overlying omentum It was "frozen" to the abdominal wall under the incision This carried the right segment of the transverse colon into close proximity to the cecum and ascending colon, to which it occasionally was directly adherent In 3 cases,

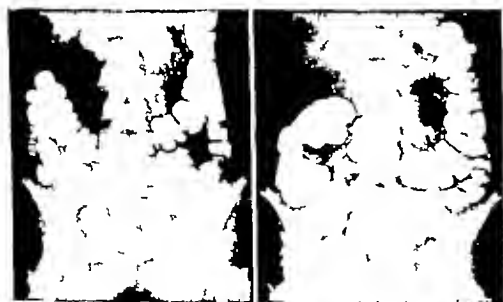


Fig 10 Case 3 Left, pre-operative, right, postoperative views Pre-operative roentgenogram disclosed active contractions, angulated hepatic flexure, colon depressed to cecum, postoperative view showed less active contractions, arching hepatic flexure, elevated transverse colon (spontaneous) Patient was a female, aged 29 years She had had an appendectomy with drainage at 17 Eleven years later onset of "dry heaves" on physical exertion, with frequent colics, severe retching and vomiting, defecation every 7 days, intermittent distention Scrubbing floors started colic At operation adherent omentum released hysterectomy for pelvic inflammation Immediate relief Bowels move daily



Fig 9 Case 2 Left, pre-operative, right, postoperative views The pre-operative roentgenogram showed a dilated, elongated transverse colon, with double angled loop The postoperative film showed smaller lumen, spontaneously shortened transverse colon, and single loop Patient was a female, aged 31 years, who had had a left adnexectomy at 22 After 8 months she had spells of colic, distention, and vomiting Intense pains were induced with enemas or movements She had an 11 weeks' spell of extreme distention, persistent vomiting, and obstipation Walking or stretching leg caused colic She lost 60 pounds At operation the adherent omentum was released and upfolded Spasm of bowel was visible Result 75 per cent improved although there was some persistent vomiting but no colic or distention Bowels were regular She gained 15 pounds

15 per cent, the displacement of the colon was to the left

Additional direct observations of distortion and dysfunction of the transverse colon were made at the operating table In 3 cases taut



Fig 11 Case 4 Left, pre-operative, right, postoperative views The pre-operative roentgenogram showed a dilatation, diminished haustra, colon depressed in pelvis, curved left segment The postoperative film showed a reduced lumen, more normal haustra, colon elevated (spontaneously), angled left segment Patient was a female, aged 19 years Appendectomy was performed when she was 16 She had immediate right lower abdominal colics Eating or rising from bed doubled her over with pain She stopped eating much because of pain She was not constipated (1 of 2 cases) but occasional diarrhea At operation the adherent omentum was released and upfolded She was relieved of all symptoms and the bowels became regular



Fig. 3 Case 5. Left, pre-operative; right, postoperative films. The pre-operative film showed an elongated, dilated colon fixed in the pelvis with sharp angulation. The post-operative film showed spontaneously shortened colon with smaller lumen, elevated from pelvis and with no angulation. This case is reported here in detail. This is one of few instances in which the gastrocolic omentum as reeved. She had complete relief of all symptoms.

bands of fibrosed omentum passed from the involved segment of the transverse colon to the low incision under sufficient tension to angulate it. In 2 of these the proximal segment of colon was grossly distended with gas, and the distal segment was collapsed. In the third case there was a large obstructing fecal impaction proximal to the angulating band. Another case showed an extreme, abnormal looping of the colon with fixation of the loop to ascending colon. Another revealed a gross



Fig. 4 Case 6. Left, pre-operative; right, postoperative films. In the pre-operative film is seen an oblique line to transverse colon, from hepatic flexure to left lower abdomen, colon is elongated and splenic flexure is lower than hepatic. In the postoperative film is shown horizontal passage (spontaneous shift) of transverse colon from hepatic to splenic flexure, shortened colon (spontaneous), splenic flexure now the higher. Patient, a female, aged 34 years, who had had an appendectomy at 8. She had mild symptoms of crowding from gas, distention, constipation. Enemas caused intense colics. At operation small tongue of fixed omentum, as found to displace the colon, but not to fix it firmly. This accounted for the mild symptoms. Operation gave relief. She also had hysterectomy for small fibroids.

angulation in the middle of transverse colon where the adhesions pulled it deeply into the pelvis. Two showed transient, firm localized spasm in mobilized segment of transverse colon after operative release of the adhesions a condition foreign to the normal colon.



Fig. 4 Case 7. Left, pre-operative; right, postoperative films. The pre-operative view shows flattened transverse colon, distortion of the hepatic flexure, and extremely hyperperistaltic. The postoperative view shows curved looping colon arching hepatic flexure, normal haustra. Patient was female aged 55 years. Appendectomy as done when she was 3. She was admitted with diagnosis of bowel tumor. One year after first operation she suffered sharp colics and constipation. She had bimonthly spells of colic, bloating, obstipation, vomiting, and was confined to bed. Walking caused colic. Operation consisting of release and resection of adherent omentum gave complete relief of symptoms and bowels moved daily.



Fig. 5 Left, Case 8; right, Case 9. Physiologic evidence. Case 8—dilatation of bowel elongation, diminished haustrations. In Case 9 there is the likely dilated lumen of bowel, coincident with obstruction-like episode. There was an apparent functional disturbance of similar nature in all segments of the bowel. Roentgen report said it suggested obstruction but it is called "colitis." Case 9 there is extreme dilatation of all portions of colon, particularly of transverse colon, with complete disappearance of haustrations. This roentgenogram taken during an obstruction-like episode, had roentgen report of obstruction of unknown origin, because the lumen of the lower colon was patent.



Fig 16 Physiologic evidence, No 2—hyperperistalsis—Case 7, No 3—segmental spasm—Case 14. In Case 7, left, we note excessive contractures of the colon with appearance of an abnormal number of deep haustrations. The overactive state is most apparent in the transverse colon although the appearance of hyperactivity carries over into the other segments. The descending colon is spastic. In Case 14, right, we note spasm in entire segment of descending colon, unaccompanied by any evidence of hyperactivity in other segments of the colon. The overspread of dysfunction into other portions of the colon than the transverse colon is suggested by this study. Spasm disappeared after surgical release of omental adhesions, and the clinical symptoms were relieved.

#### PATHOLOGICAL PHYSIOLOGY

Complete pre-operative and postoperative roentgen studies made in 20 of the cases yielded evidence of dysfunction of the colon in 14 of them, 70 per cent. Eight criteria of dysfunction noted may be grouped under two major subdivisions—the physiological and the anatomical evidences of dysfunction.

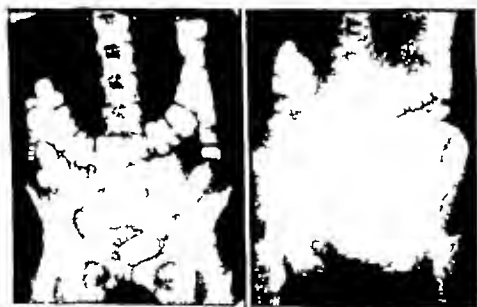


Fig 18 Physiologic evidence, No 4—focal spasm—Case 3. Left, pre-operative postero-anterior roentgenogram taken in horizontal position without traction, showing absence of spastic areas which appear in the film at right with traction. In 6 films taken before operation without traction and after operation with traction, there was always absence of spasm. Right, areas of spasm in transverse colon due to traction from omental adhesions when patient is put in Trendelenburg position. This may indicate the mechanism of production of pain upon exertion, whereby the fixed omentum pulls and irritates the bowel.

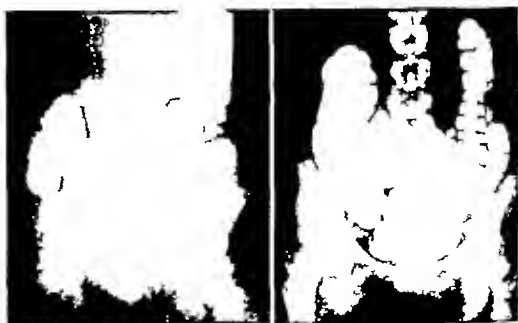


Fig 17 Physiologic evidence, No 4—focal spasm. In Case 22, left, we note spastic area at point of fixation of the right portion of the transverse colon by omental adhesions. This observation was made during an operation for another condition, and the roentgenogram was then taken after operation on a positively proved lesion. The roentgenogram at right, Case 2, was taken after an effort to expel the barium clyisma. This resulted in a drop of the unfixed left portion of the transverse colon into the lower abdomen, with persistent fixation of the elevated right portion. At the juncture of these two segments is a spastic area which also was visualized at the operating table, when the adherent bowel was released.

*A Physiological evidence* (1) Dilatation, diminished haustrations, and elongation of the transverse colon, sometimes interpreted as "colitis" and obstruction, were noted in 8 cases. (2) Hyperperistalsis occurred in 2 cases. (3) Segmental spasm was seen in 2. (4) Focal spasm occurred in 5. (5) Delayed emptying was evidenced in 5 cases by the markedly increased capacity of the colon to empty a

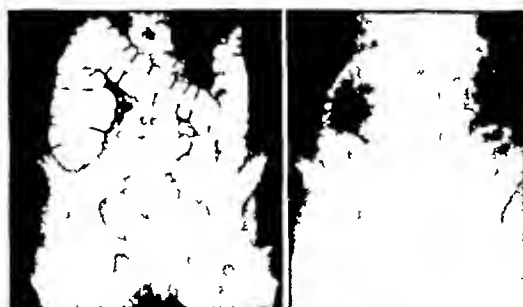


Fig 19 Case 6. Pre-operative, left, and, right, postoperative films showing physiologic evidence, No 5—delayed emptying, (a) barium enema. High grade retention of barium enema in the pre-operative roentgenogram, as compared with the efficient emptying seen in the postoperative roentgenogram, after lysis of omental adhesions. Note different placement, after operation, of transverse colon, which is a spontaneous shift following lysis of adhesions. There were only mild clinical symptoms in this case, even with marked displacement, because of the very limited fixation of the colon.





Fig. 30. Case 1. Pre-operative, left, and, right, post-operative films showing physiologic evidence, No. 5—delayed emptying. (b) motor meal. Forty-eight hour retention of barium in right half of colon. This plate taken at 24 hours, displaces exactly the fluoroscopic finding at 48 hours. Not excess gas in bowel. Quick emptying of motor meal following release of oriental adhesions. Part of barium passed by rectum in 4 hours. This 24 hour plate shows nearly complete clearance of all barium from bowel. Not absence of gas.

claysms following release of the adhesions. 3 patients showed extreme delay in the transit of a barium meal from the cecum to the rectum up to 96 hours late retrograde transport of barium in the colon many hours after ingestion indicated that this delay may be due to reverse peristaltic waves.

**B Anatomical evidence.** Abnormal anatomical conditions were noted from which a consequent dysfunction may be fairly inferred. (6) Angulation, sufficient to impede emptying was noted twice. (7) Loop formation, of an extreme degree was observed once. (8) Fixation of the right transverse colon as noted under the fluoroscope in 8 cases. 40 per cent was verified by 3 methods. (a) pressure dis-

placement, by which compression and lateral displacement of the abdominal wall carried the fixed colon laterally with it. (b) segmental fixation by which the right transverse colon remained fixed while changes in position caused a shift in the position of the free left transverse colon. (c) traction displacement by which traction on the incision by adhesive strips fixed over the incision caused measurable shifts in the position of the fixed portion of the colon. Roentgen and operative observation never showed displacement of the stomach.

Correlation of these clinical and roentgen observations with known facts of gastrointestinal physiology convincingly establish this syndrome. The normal caudad transport of aliment is regulated as shown by Alvarez through gradients of activity in the bowel. There is a heightened intensity of rhythmicity, tone and irritability in the upper bowel as contrasted with the lower bowel. This insures transport of chyme downward in the same way as the head of pressure at the spigot drives water through a hose to its nozzle. Also important in regulating gastro-intestinal activity is the gastrocolic (ileogastric) reflex described by Macewen (1904) and restudied by Hurst (1913). A neural interrelationship is established by this extrinsic nerve reflex between the stomach and the ileocecal region. By it the activities of these widely separated segments profoundly influence each other. i.e. the intake of food increases the rate of discharge of ileal contents into the colon and conversely irritability in the ileocecal region



Fig. 31. Case 8. Physiologic evidence, No. 5—delayed emptying. (b) motor meal. Extreme delay in passage of barium through the colon due to dysfunction from oriental adhesions. Part of meal in cecum.



b, 48 hour progress, meal delayed in transverse colon. c, 72 hour progress, meal has reached descending colon. Note excess of gas in proximal colon. d, 96 hour at which time the meal has finally reached the rectum.

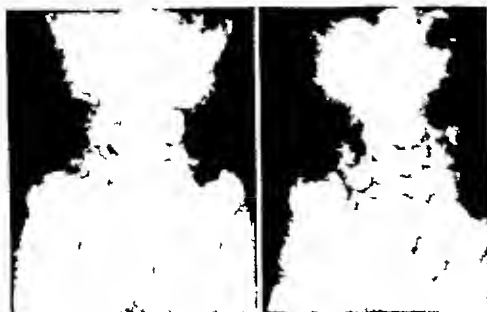


Fig 22 Physiologic evidence No 5—delayed emptying, (c) late retrograde transport (barium by mouth) Case 19. Left, at 48 hours three globules of barium have entered the distal left half of the transverse colon with part of the mass overlying, and part to the left of the spine. Right, at 72 hours these same masses have been carried back towards the right of the spine where they have been brought up against the angled portion of the fixed right portion of the transverse colon. This case at 120 hours showed reflux of barium back into the cecum. Note excess of gas.

disturbs gastric motility, causing nausea and vomiting. Disorders in the functioning of the tract arise from disturbances of these two factors. First, a reversal of the gradients of activity by an irritant causes waves of reverse peristalsis which pass cephalad to the stomach and terminate in nausea and vomiting; second, abnormal stimulation of the gastrocolic reflex by an irritant in the ileocecal region produce

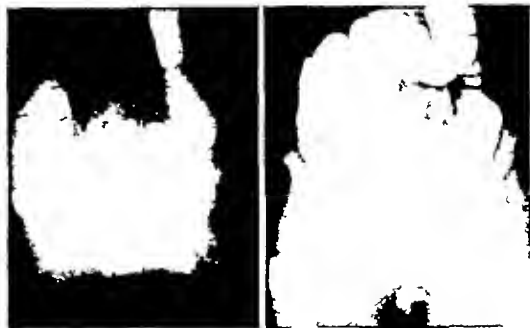


Fig 23 Anatomic evidence No 6—angulation—Case 5, No 7—loop formation—Case 18. Left, Case 5 shows two arms of the transverse colon descending deeply into the pelvis so as to form an acutely angulated loop, fixed deeply in the pelvis. At the operating table the two arms were adherent to each other with their apex showing such an abrupt turn as to create an obstructing angulation. Right, Case 18 shows an excessively redundant loop of a tremendously dilated transverse colon. The midportion of the transverse colon approximates the hepatic flexure and forms a loop down the full length of the ascending colon and up to the hepatic flexure. The arms of the loop were adherent to each other and to the ascending colon by pathologic postoperative omental adhesions.

irregularities in gastric function which are made manifest by nausea and vomiting—the most dramatic evidence of low bowel dysfunction.

Integration of these clinical, roentgen, and physiological data explains the dysfunction.

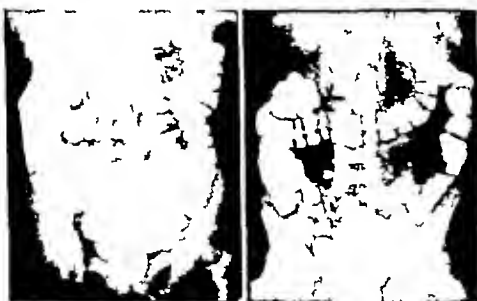


Fig 24 Anatomic evidence No 8—fixation of colon (a) pressure displacement. Left, anteroposterior exposure showing fixed right loop of transverse colon close to midline, and only slightly encroaching on the ascending colon. Left half of transverse colon well over to the left overlying the descending colon. No evidence of hyperperistalsis. Right, postero-anterior position, showing marked displacement of right loop of transverse colon to outer border of ascending colon from pressure displacement, with the abdominal wall. Also left portion is drawn away from descending colon. Hyperperistalsis, presumably from traction of the omentum, has appeared in the right portion of the transverse colon.

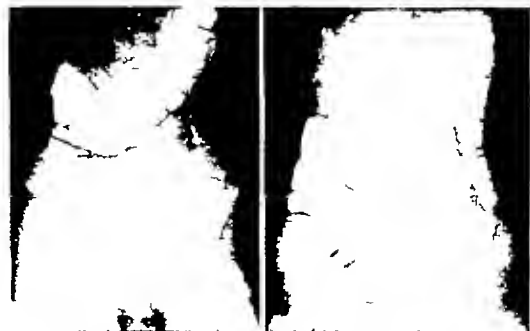


Fig 25 Anatomic evidence No 8—fixation of colon, (b) segmental fixation—Case 23. Left, supine position. There is a normal curvature in the outline of the transverse colon. This routine posteroanterior roentgenogram gives no suggestion of a fixation of the transverse colon. Right, Trendelenburg position. When the position is altered so that the head is down, the free left portion of the transverse colon is thrown into the upper abdomen. At the same time the right portion is held fixed and angulated by omental adhesions. Case 2 (physiologic evidence No 4) shows a similar fixation of the right half of the transverse colon when the left half dropped into the pelvis on evacuating the clysmas.



Fig. 26. Anatomic evidence: \ — fixation of colon, ( ) traction displacement. Left: traction upward on adhesions fixed over the iliac crest. Hepatic flexure near the top of the second lumbar vertebra lateral to it. Loop of right transverse colon: 1 level of the lower border of the fourth lumbar vertebra, on line with the iliac crest. Right: traction downward. By use of contrast hepatic flexure has dropped to the top of the third lumbar vertebra overlying it. The loop of right transverse colon is down to level of the lower portion of the fifth lumbar vertebra, far below the level of iliac crest across the iliac crest.

arising from omental adhesions. The irritating effect of omental adhesions on the colon has been noted clinically and by roentgen study. Clinically, the pull of the adhesions from exercise, stretching, extending the leg driving an automobile, kneeling, washing the floor, walking, established a degree of irritability which announced itself locally by colic, and reflexly by nausea and vomiting, serious falls, producing a tearing sensation in the region of the adhesions, were followed by prolonged intense colics. Roentgenograms taken when traction was purposely produced on the colon via the omentum showed spasm which was not present in the absence of traction. 30 per cent of the pre-operative roentgenograms showed dilatation and diminished haustrations called colitis. 20 per cent showed a toneless elongation of the transverse colon which disappeared following release of the adhesions. Apparently from restored tone. 30 per cent showed heightened irritability as manifested by local or segmental spasm or general hyperperistalsis. 25 per cent showed evidence of delayed emptying of the colon. 15 per cent showed late retrograde transport of barium. Gross visual evidences of dysfunction noted at the operating table were: excessive distention by gas of the segment of colon proximal to the adhesions; impaction of fecal matter proximal to the



Fig. 27. Case 20. a. In 1935, patient's weight 50 pounds. Hysterectomy years before in 1933. Per rectally all, eating, no pain, bowels regular. b. In 1937 she weighed 75 pounds. For year spells of colic, vomiting, and progressive constipation, with severe irritant distention. Beginning obstruction-like episodes. c. In 1940, her weight as 5 pounds. Repeated hospitalization for obstruction-like episodes, with reflex vomiting. Total incapacity from colic, vomiting, constipation. Operated upon for omental adhesions. No other disease demonstrable after repeated roentgen studies and laparotomies. Patient died in May 1941, 4 years after onset of the syndrome, from inanition, exhaustion, and terminal pneumonia.

fixed angle of the bowel, transient marked spasm in the released segment of colon. From this demonstrated irritability in the colon arose the clinical manifestations of dysfunction—Intractable constipation, chronic colic, distention and borborygmi, reflex nausea and vomiting. This irritability was stimulated by normal functional activities: the intake of food and the act of arising from bed in the morning stimulated a discharge of chyme from the ileum into the cecum which caused hyperactive irritability in the adherent bowel as manifested by intense colics and reflex vomiting, initiation of peristalsis by spontaneous bowel movement or injection of an enema, produced excruciating colic and sometimes vomiting. Thus so accurately do the clinical and roentgen observations integrate with the established facts of gastro-intestinal physiology as to justify presentation of this clinical picture as a specific syndrome having an adequate physiological background.

## TREATMENT

Prevention of the lesion is of paramount importance. In operative procedures through low abdominal incisions, particularly in female patients in the early decades of life, all trauma to the omentum and peritoneal edges must be sedulously avoided, the omentum must never be caught in the suture line, a high lying omentum must never be pulled into the lower abdomen during the final peritoneal toilet, the peritoneum is best closed by a running mattress suture which produces ectropion of the rough edges, postural drainage by head blocks is preferable to Fowler's position, which crowds the omentum into the lower abdomen.

The surgical release of the omental adhesions is usually best accomplished through a low incision in close proximity to the adhesions. Occasionally, following multiple operations, or with roentgen evidence of ptosis of the colon requiring a reefing of the gastrocolic omentum, a high incision is preferable. Following release of the adhesions, three procedures proved valuable in preventing recurrence of the lesion, (1) resection of the released, fibrosed segment of omentum, (2) unfolding the omentum and fixing it with sutures to the gastrocolic omentum, (3) reefing the gastrocolic omentum, in the presence of marked ptosis, so as to elevate the bowel from the lower abdomen.

Further radical measures were attempted in 3 cases which suffered recurrence of incapacitating symptoms. Ileosigmoidostomy was first tried but it failed to bring relief because of a roentgen demonstrated reflux of barium back to the cecum past the adherent, irritable bowel. Right colic exclusion (transection of the transverse colon with stoma drainage of right half, left ileo-transverse-colostomy), thus isolating the irritable right colon from the functioning intestinal tract, was then tried. One patient showed no improvement, while 2 were improved about 50 per cent. These few cases do not permit evaluation of this method. Apparently there always will remain a small residuum of victims harboring vicious omental adhesions, to whom neither the internist nor the surgeon can bring lasting relief. During the postoperative period, in addition to routine postoperative care, elevation of the foot of the bed on blocks will carry the released

bowel into the upper abdomen away from the peritoneal tags from the released omentum. Amfetin was sometimes used.

## ANALYSIS OF STUDY

The preponderant incidence of this disease among women is striking. Wherever noted, the sex of all cases reported in the literature was female. In this series, whereas 20 women, 85 per cent, were operated on, only 3 men, 15 per cent, were encountered. After excluding 6 pelvic operations, there was an etiological incidence of 14 appendectomy incisions among women as against 3 appendectomy incisions among the men. Except in terms of a constitutional sex factor, this extreme discrepancy between the sexes in the ratio of 4:1 is not easily explainable. Possibly the higher incidence of a ptotic habitus and low lying colon and omentum among women has some bearing on this anomaly.

Analysis of the age relationships is instructive. The primary operation which caused the adhesions was performed at an age under 20 years in 12 cases, during the twenties in 7 cases, during the thirties in 3 cases, after 50 years in 1 case, excluding the last case the average age at the time of the primary operation was 20 years, making the lesion a surgical hazard of youth. The time interval between the primary operation and the onset of symptoms ranged from a few months to 19 years, averaging  $3\frac{1}{2}$  years. The duration of suffering between the onset of symptoms and the current lysis of adhesions ranged from 2 to 18 years, averaging 8 years. The current operation was performed at an average age of 33 years, the youngest patient being 17 years of age, and the oldest 67. Interval operations had been performed with no relief in 12 patients, 50 per cent of the group, with the sacrifice of many innocent organs, chiefly the gall bladder and pelvic organs, 5 patients had 1 interval operation, 2 had 2 operations, 2 had 3 operations, 2 had 4 operations, 1 had 6 operations—a grand tally of 29 unsuccessful interval operations.

The etiological significance of infection as compared with aseptic trauma, in causing these adhesions, does not appear as impressive in this series, as it did in the study by Muller

and Rademaker. In 16 of the present cases characterized by but one or two operations before the current lysis of adhesions, all hospital records were available for study. Analysis of the factors of operative trauma and infection grouped these cases naturally into 3 divisions. In the first subgroup there were 10 patients who were subjected to clean surgical procedures: there was no infection at the time of operation, the peritoneum was closed without drainage, the postoperative course was uneventful, with no unusual febrile reaction; the patients were discharged early, with cleanly healed incisions. Only the factor of aseptic trauma may be fairly incriminated in these cases. In the second group there were 3 cases in which operation was done for acute appendicitis. There was no recorded infection of the peritoneal cavity at the time of operation, and drainage was not instituted; the incision healed cleanly by first intention; the patients were discharged early. Although infection may have played a minor rôle in this group, certainly operative trauma appears to have been the major factor in causing these adhesions. The third group presenting frank records of acute suppurative appendicitis with peritonitis, for which drainage was carried out, contained only 3 cases. Infection in this group was probably the dominant factor in causing adhesions. In summary, an evaluation of the factor of aseptic operative trauma versus infection as the causative agent of symptom producing omental adhesions, indicates, that in 60 per cent of the cases, the adhesions resulted from aseptic operative trauma; that in 23 per cent they were due to aseptic trauma predominantly, with a minor element of infection; and that in only 17 per cent was the formation of adhesions due primarily to infection.

Diagnosis may be difficult if all the components of the syndrome are not present. In this series, the reflex symptoms, sometimes appearing late, were elicited from all but one patient; the elements of the colon complex were always present in part or entirely; peritoneal symptoms were noted in 13 instances, denied in 3 and not recorded in 7. In the present series a pre-operative diagnosis was achieved in 17 of the 23 cases, 74 per cent,

frequently by other physicians acquainted with this study. In differential diagnosis this lesion is widely disregarded. It is confused with gall bladder ulcer and pelvic diseases, and postoperative hernia. The most difficult differentiation is between omental adhesions and small bowel adhesions. The cyclical recurrence of obstruction-like episodes characterized by the early reflex vomiting of stomach ingesta, usually with spontaneous subsidence of the condition, is the chief distinguishing characteristic of omental adhesions. "Effort" or "traction" colic, as well as the predominant "colon" features in the story, balance the differentiation more toward omental adhesions. "Focal vomiting instead of reflex vomiting almost commits the diagnosis to small bowel adhesions. Doubtlessly many clinical reports of satisfactory conservative management of intestinal obstruction include cases experiencing the cyclical exacerbation of symptoms from omental adhesions, unrecognized in the absence of surgical exploration; also it is quite possible that poor results following an apparently satisfactory technical management of small bowel adhesions may represent persisting symptoms from coexisting omental adhesions, not evaluated or corrected at the time of operation. The chief offense is labelling these sufferers psychoneurotics, as was done in 14 of the cases. Probably many functional diagnoses of atonic or spastic constipation, colitis, irritable colon, functional indigestion—all fortified by negative roentgen reports—represent inadequate evaluation of the second or any functional manifestations of omental adhesions.

The results of operative intervention—granting 25 per cent each for the four major complaints, such as colic, constipation, distention, and vomiting—show in the final summary of 20 completed cases: 12 patients, 60 per cent, completely relieved; 2 patients, 10 per cent, 75 per cent improved; 4 patients, 20 per cent, 50 per cent improved; 2 patients, 10 per cent, entirely unrelieved. One patient died from unexplained intestinal obstruction unrelieved by ileostomy. Another patient was followed for 4 years to the final outcome of death from recurring spells of vomiting, from debility and inanition. The surgical failures

among these "omental cripples" are a source of oppressing concern to the surgeon who must watch their hapless invalidism

### CONCLUSION

A surgical experience with 23 cases of symptom producing omental adhesions, unrelieved by medical care, has yielded clinical, pathological, and roentgen data not previously published in the literature. These data appear to justify this presentation of a specific syndrome based on a dysfunction of the transverse colon, induced by pathologically fibrosed, adherent omenta, fixed under tension to a low abdominal incision.

I wish to express my indebtedness to Dr. Andrew E. O'Connell for his patience in carrying out repeated roentgen studies in this unpromising group of patients.

### BIBLIOGRAPHY

- 1 ADAMI, The great omentum, Phila. M. J., 1898
- 2 ALVAREZ, W. The Mechanics of the Digestive Tract, New York, Paul B. Hoeber, Inc., 1928
- 3 BRAQUEHAYE, J. Bull. de l'hôp. civ. franç. de Tunis, 1900, III, 204-248
- 4 BROWN, LER. Am. J. Obst., 1912, 65, 480
- 5 CLARK, J. G. Surg., Gynec. & Obst., 1909, 9, 603-607
- 6 COLLINS, F. K. Calif. & West. Med., 1929, 28, 179-182
- 7 CRAIG, D. H. Am. Med., 1903, 6, 438
- 8 FISHER, Bnt. M. J., 1906, 1, 235
- 9 FLOREY, H., and CARLETON, H. M. J. Path. & Bacteriol., 1926, 29, 97-106
- 10 GOMEZ DE ROSAS, N. Rev. méd. cubana, Habana, 1924, 35, 204-207
- 11 GREGOIRE, Quoted by Pilven
- 12 HAMILTON, Australas. M. Gaz. Sydney, 1913, 33, 619
- 13 HAUG, Muenchen. med. Wchnschr., 1923, 70, 463
- 14 HERTZLER, A. E. J. Am. M. Ass., 1913, 60, 1292
- 15 Idem, Tr. West. Surg. Ass., 1916, 26, 99
- 16 Idem, The Peritoneum, Vol. 1, p. 309, St. Louis, C. V. Mosby Co., 1919
- 17 HOWITZ, I. Kjöbenhavn, med. Selsk. Forh., 1888-89, 112
- 18 Idem, Kjöbenhavn, med. Selsk. Forh., 1893-94, 23-24
- 19 HURST, A. F. J. Physiol., 1913, 47, 54-56
- 20 LARKIN, C. L., and BURNHAM, N. G. New England J. Med., 1940, pp. 208-213
- 21 LADWIG, A. Arch. f. klin. Chir., 1928, 1, 151
- 22 MACEWEN, W. Lancet, 1904, 2, 995-1000
- 23 MORRISON, Bnt. M. J., 1906, 1, 76
- 24 MULLER, G. P. Pennsylvania M. J., Athens, 1913-14, 17, 621-625
- 25 MULLER, G. P., and RADEMAKER, L. A. Arch. Surg., 1933, 26, 208-287
- 26 NEUHOF, H., and WIENER, S. Surg., Gynec. & Obst., 1910, 11, 348-349
- 27 PILVEN, M. J. Bull. et mém. Soc. de chir. de Par., 1925, 51, 35-37
- 28 SCHUTZ, C. B. Surg., Gynec. & Obst., 1930, 50, 541-544
- 29 WALTHER, Bull. et mém. Soc. de chir. de Par., 1905, 31, 396-399
- 30 WHITE, P. A., and GARSIDE, A. A. Illinois M. J., 1931, 59, 124-125

## THE INTRA ABDOMINAL APPLICATION OF SULFANILAMIDE IN ACUTE APPENDICITIS

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THIS paper is an analysis of acute appendicitis at the Roosevelt Hospital during the 6 year period of 1935 to 1940 inclusive the first 5 years represent an average background against which we hope to contrast the results of those cases during 1940 in which patients were treated by the intra-abdominal application of sulfanilamide.

Full credit must be given to the two men responsible for the first use of the drug at our hospital. First to Dr. R. Sterling Mueller who had the courage to sprinkle copious quantities into the peritoneal cavity in what seemed a hopeless case of peritonitis and second to Dr. William H. Casebaum, who leaning over his shoulder at the time of operation collaborated in the idea. The procedure was taken up immediately by one and then another of our surgical staff and now is routine when indicated.

To make a thorough analysis of this sort requires a great deal of careful, and frequently tedious, work tabulating facts garnered from histories for later interpretation. The histories of over 1000 cases during the 6 year period were reviewed in order to include only those cases of definitely acute appendicitis. We then eliminated several hundred borderline cases and others which were definitely not in this strict classification. Those thrown into the discard included cases of acute catarrhal interval, subsiding acute, chronic, and mechanical varieties cases of acute mesenteric lymphadenitis and frequent ones reported by the pathologist as showing either fibrosis or a normal appendix.

Our series thus represents, as accurately as it was possible to determine the distinct group of acute suppurative appendicitis known

in operating room jargon as the 'red hot appendix.'

The surgical concept of the signs and symptoms, and the diagnosis of acute appendicitis has changed little in the past three decades but there have been great advances in the surgical technique. The mortality rate has continued to be sizeable in spite of these improvements, and periodically we are alarmed with reports that it is on the increase. In an effort to lower this rate, every encouragement should be and is given to any safe method which will accomplish this end.

The management of this condition at the Roosevelt Hospital has not changed since 1935 except in relationship to the use of sulfanilamide. We consider every case to be an acute surgical emergency, whether it be day or night. We do not believe in the conservative treatment of peritonitis and delay operation only long enough to replenish fluids, electrolytes, or blood proteins where such treatment is believed to be indicated. The occasional patient is seen, however, in such a critical state that even the slightest trauma under local anesthesia would be fatal; here we recommend delay and transfusions. Two such instances occurred during the 1935 to 1939 interval: one patient died within a few hours and the other improved sufficiently to be operated upon at the end of 24 hours, only to succumb later.

A case diagnosed as appendiceal abscess when patient is admitted to hospital is delayed if the operator feels the localizing process has been completed but when doubt exists, immediate operation is believed to be safest.

The McBurney incision is routinely employed whenever the diagnosis of acute appendicitis is made and we feel that it has been largely responsible for a nominally low mortality rate. It was used in about 95 per cent of our cases.

From the Surgical Services of the Roosevelt Hospital, New York, N. Y.

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The appendix is removed by cautery or the phenol knife and inverted with a linen purse-string suture re-enforced by a Lembert of cat-gut without ligating its base. Simple ligation of the base without inversion of the stump is reserved for those patients with inflammation and resultant thickening of cecal wall, or if application of the pursestring is technically difficult.

In the presence of an appendiceal abscess, when exposure and removal of the appendix increase the possibility of spreading the infection to uninvolved peritoneum, simple incision and drainage are employed with the intention of secondary appendectomy at a later date. Otherwise the appendix is removed and the wound is closed about one or two drains. The soft rubber fenestrated tube has been the drain of choice, since we believe that the establishment of a tract can be obtained best in this manner.

In the presence of peritonitis the usual procedure is to place a drain down to the pelvis and another to the site of the appendix stump. The peritoneum is rarely closed without drainage.

In the simple acute case the wound is closed in layers without drainage, in cases of doubtful localized peritonitis a soft rubber tube or Penrose drain is placed down to peritoneum and the abdominal wall is closed singly about the emerging drain.

The great majority of patients requiring drainage of the peritoneal cavity have been closed after the manner recommended by Dr. John Garlock, which consists in simple closure of the peritoneum about the drains, with the remainder of the wound left wide open. A few of the surgeons have approximated transverse muscles and internal oblique muscles in addition.

In an analysis of such a series of cases as we are presenting, certain criteria must arbitrarily be chosen to classify the various types of lesions so that they may be easily and clearly understood as well as easily and accurately compared with similar groups. It is for this reason that we eliminate the many confusing terms and classify this series of cases of acute appendicitis as recommended by Dr. Mont R. Reid.

**Group 1** The simple acute appendicitis. In this variety there is no gross evidence of perforation, the fluid about the appendix if present is not frankly purulent, and a culture of such fluid if taken has been reported as showing no growth.

**Group 2** The acute appendicitis with localized abscess formation.

**Group 3** The acute appendicitis with peritonitis. This final group includes both those cases of spreading or diffuse peritonitis and those of the localized variety. It is believed that a true knowledge of the extent of a peritonitis is impossible to obtain through an ordinary incision. The impression would vary with the individual surgeon and could be accurately determined only after a very improper operation (6).

In most instances the operator's vivid description of the peritonitis left no doubt that it belonged in this group, but occasionally his description was doubtful and, in such an instance, dependence was placed on a positive culture. When a culture of peri-appendiceal fluid was reported positive for *Bacillus coli* or streptococcus, even though no gross perforation was detected and even if the appendicitis had been described as the simple acute variety, we classified it as a case of localized peritonitis. In the cases of abscess formation or peritonitis, we found that *Bacillus coli* was the causative organism in 83 per cent of cases. Other organisms encountered as etiological factors in their order of frequency were gamma streptococcus and beta streptococcus. Sometimes associated with *Bacillus coli* or with the streptococcus organisms were *Bacillus proteus*, *Bacillus lactis aerogenes*, and *Bacillus mucosus capsulatus*. No anaerobic cultures were done.

In January, 1940, we began using sulfanilamide crystals placed directly into the peritoneal cavity as an adjunct in the treatment of acute appendicitis with perforation and peritonitis. The first few patients were desperately sick, the peritonitis in each instance seemed diffuse in character, and the fluid was frankly purulent and had a fecal odor. The convalescence and cure of these patients was so dramatic, that one could not help but be impressed with the value of the drug used thus.



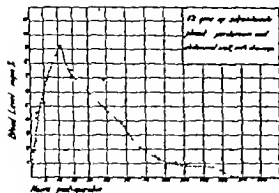


Fig. Coagulated average blood level curve. This chart includes all patients who received total of grams of sulfanilamide and on whom postoperative blood levels are taken. The number of levels taken on each patient varied from 1 to 8. None of these patients received sulfanilamide after operation by any route. Each of the points on the graph represents time indicated. From these scattered points curve is drawn which roughly indicates the rate of absorption of the drug and maintenance of the blood concentration.

The technique employed was at first rather crude, consisting in pouring the crystals directly into the depths of the wound with the retractors spread widely apart and lifted in order to give greater depth to the peritoneal cavity. The drug sterilized only by the chemical company at the time of preparation was poured directly from the frontylin bottle into a sterile 1-ounce measuring glass held by a suture nurse. If 2 drams of the drug were used, we knew by rough computation previously determined by the druggist that 5.5 grams had been administered.

We later discovered that it could be sterilized without disturbing its crystalline powdery form. The crystals were found difficult to manage the minute they struck moisture and in this respect greatly resembled sugar. A moist heat used for sterilization that can penetrate to the drug converts it into a hard rock-like mass on drying for this reason autoclaving is unsatisfactory.

The sulfanilamide is now weighed in the drug room, put into test tubes in 2, 4, 6 and 8 gram quantities and each tube snugly stoppered with cotton. The tubes are then sterilized by placing in an oven, where the heat is maintained at 120 degrees C for one-half hour.

The test tube is a handy container as it has been the most effective implement for depositing the crystals in the peritoneal cavity. An implement, such as a long handled gall-bladder scoop which allows blood serum, or peritoneal fluid to touch the drug immediately converts the soft dry powder into a wet sugary substance that clings to the applicator.

We have placed varying quantities within the peritoneal cavity. A smaller amount is often placed in the abdominal wall layers during closure as we have found wound healing aided by this maneuver in the frankly purulent cases. There is no doubt that involvement of the wound thus seems much more limited and localized to the vicinity of the emerging drain. This feature has been such a consistent finding that it is a great temptation to discard the Garlock method of closure.

Postoperative sulfanilamide blood levels have been taken at frequent time intervals. The initial rise is prompt and fairly consistent; the fall in blood level is much more gradual but shows the same consistency (Fig. 1). When the drug is put only in the peritoneal cavity and not in the abdominal wall, the fall is very abrupt. The average peak obtained was 6.9 milligrams of sulfanilamide per 100 cubic centimeters of blood, and the average time at which this point of maximum concentration was reached was 14.7 hours after operation.

The height of the original rise is entirely dependent upon the amount used and also upon the amount which is lost in the presence of a drain. The length of time in which one can expect to get a positive blood level is also markedly influenced by the presence of drains and is in direct proportion to the amount placed in the muscle and subcutaneous layers.

These findings imply that the drug is absorbed from its local storehouse at a definite rate. The greater the amount used and the less it is allowed to be lost through drainage the higher the possible blood level. It also indicates that the body absorbs the drug much more rapidly from the peritoneum than it does from the muscle or fat.

Draper and Kauer have shown in dogs that, after intraperitoneal use of sulfanilamide blood level reached its peak in about 6 hours and rapidly approached zero in 65 to 75 hours.

TABLE I

Total cases	Number of cases	
	59	145
Complication	Sulfanilamide in peritoneum	None used
Wound complication	6*	5
Prolonged temperature	7	0
Pulmonary embolus	2	3
Serum in wound	1	0
Fecal fistula (temporary)	2	0
Upper respiratory infection	1	2
Secondary peritoneal abscess	1	1
Jaundice	1	0
Atelectasis	0	3
Phlebitis	0	1
Hematuria	1	0

\*This term does not apply to cases of prolonged wound drainage, but indicates those cases showing secondary wound abscess. We feel that too much dependence was placed on the sulfanilamide in these cases, and improper drainage of the wound was performed.

It is our contention that there is a tremendous concentration of the drug locally, many times the amount represented by its blood level, and that the mode of attack against the peritonitis is much akin to an *in vitro* destruction of the bacteria.<sup>1</sup>

Postoperative blood levels have been taken in a few cases at 2, 4, 6, 12, 18, and 24 hour intervals, and subsequently at 8 o'clock each morning until the report is completely negative for any trace of sulfanilamide. In others, the levels were taken at sporadic intervals. The impression has been gained that the point of maximum absorption into the blood stream occurs at about 12 hours from the time of its introduction and then steadily declines.

The average adult dosage recommended in case of peritonitis is 8 grams intraperitoneally and 4 grams placed in the abdominal wall layers. A few grams more can be used in the treatment of severe diffuse peritonitis, and less in the treatment of the definitely localized variety. The appendiceal abscess seems to lose the drug more rapidly by drainage, and in this type it is safe to use as high as 20 grams total.

Age and weight are factors which modify dosage, in infants and children we have used one-quarter or one-half the amount employed for the adults. It is safe to calculate the dos-

TABLE II —COMPARISON OF IMPORTANT COMPLICATIONS

Type of complication	1935-1939 (741 Cases)		1940 (204 Cases)	
	No	Per centage of total cases	No	Per centage of total cases
Wound infection	85	11.5	11	5.4
Secondary peritoneal abscess	21	2.8	2	0.9
Atelectasis	16	2.1	3	1.4
Pneumonitis	12	1.6	0	0
Wound separation	8	1.1	0	0
Phlebitis	5	0.7	1	0.5
Pylephlebitis	2	0.27	0	0
Jaundice	1	.13	1	0.5

age on a basis of 175 milligrams per kilogram of body weight.

One of the patients with abscess had a secondary appendectomy about 2 months later. The lack of adhesions encountered and the normal appearance of the peritoneum were striking. This one example adds to our general impression that the drug does not irritate the peritoneum.

We have noticed no definite toxic effects from the use of the drug administered in this fashion except some cyanosis, which, though not a constant feature, is usually evident. The nausea and vomiting, if present, have not been sufficiently distinguishable from that to be expected in a convalescent from an appendectomy.

There have been no cases of leucopenia or agranulocytosis, but there was 1 case of jaundice which was felt to be secondary to the streptococcus peritonitis, as it disappeared under the continued administration of sulfanilamide by mouth (Table I).

Persistent elevation of temperature did occur in a few instances, and in several of these cases it was felt directly attributable to the sulfanilamide.

In those patients in whom sulfanilamide was used the age varied from 1 to 72 years. The lesion in 45 per cent of the peritonitis group could definitely be considered diffuse. Many of these patients were critically ill, and in a few the constitutional condition of the patient and the local findings presented a

<sup>1</sup>The Winthrop Chemical Co. Inc. informs us that from 157 to 160 grams of sulfanilamide will dissolve in 100 cubic centimeters of beef serum at 37 degrees C. This approximates what one might expect to take place within the peritoneal cavity in the human and would give under these circumstances a concentration of about 1600 milligrams per cent.

TABLE III  
1935-1939

	Cases	Deaths	Mortality %
Acute	566	3	53%
Chronic	59	4	6.7%
Total	625	7	1.1%

clear picture. We feel that the cure in these instances was nothing short of miraculous.

Salicylamide was used in a total of 59 or per cent of the cases, representing each one of our three groups of the disease. In all of these 59 instances it was continued either by rectum or by mouth because of the extremely severe pathological process encountered at operation or the continued critical condition of the patient. The added experience with dosage has led us to believe that a sufficiently large intra-abdominal application eliminates the necessity for any continued operative administration.

## RESULTS

During the 1935 to 1939 period a total of 625 patients with acute suppurative appendicitis were operated upon, with 7 deaths, a mortality rate of 1.1 per cent (Table III). A further analysis of these deaths can be obtained from glancing at the accompanying Table (Table IV) but needless to say the majority were directly attributable to peritonitis. Of the 3 deaths which occurred in the acute group they give a mortality rate which although has been reported considerably lower for this group by other clinics (Table V). One of these deaths was due to a bad rheumatic heart, one to pyelonephritis and septicemia,

TABLE IV—ANALYSIS OF DEATHS  
1935-1939

	Cases
A. Diffuse peritonitis	1
B. Post operative pneumonia	1
C. Pyelonephritis and septicemia	1
D. Pulmonary embolism	0
E. Rheumatic heart and decompensation	0
F. Acute pericardial cystitis	0
Total	3
Acute	A+C+E = 3
Chronic	A+B+C+F = 4
Peritonitis	A+B+C+F = 3

and the third to poor surgical judgment, as an inadequate operation had been performed.

The mortality rates for the abscess and peritonitis group are low as compared generally with statistics from other hospitals.

During 1940 we treated a larger total number of patients with appendicitis than had ever been treated in any previous year (Table VI). This is directly attributed to the fact that it is our first full year with an ambulance.

The proportionate number with abscess and with peritonitis was the same, but the actual number was greater than in any previous year. As a result, we dealt with more critical cases of peritonitis during this period.

There were no deaths from the disease in any one of the three varieties, the impressive mortality rate of zero. Complications were relatively few in the total series (Table I) and there was a noticeable reduction in wound infections and secondary peritoneal abscesses, as compared to the previous years (Table II).

## SUMMARY

A total of 741 patients with acute appendicitis was operated upon during the 1935 to

TABLE V—COMPARATIVE MORTALITIES FROM OTHER HOSPITALS

	Acute Cases	Mortality %	Abscess Cases	Mortality %	Peritonitis Cases	Mortality %	Total Mortality %
C. et al. Cook County Hospital	639	1.1	—	—	284	12.8	—
Ward and Brown, Johns Hopkins	533	—	26	—	96	14.52	6
Ward and Ochsmere, Cherry Hospital, New York	266	6	—	—	179	17	—
Ward and Montross, Cincinnati General Hospital	36	—	19	20.52	209	17.22	26
Ward J. B. Jr. Richmond, Va.	706	—	—	—	23	26	95
Ward and McLaughlin, Omaha, Nebraska	164	—	30	—	224	—	—
Ward Hospital, New York City, 1931-40	728	4.2	20	1	12	—	—

TABLE VI — 1940

Type	Cases	Deaths	Mortality %
Acute	152	0	0
Abscess	21	0	0
Peritonitis	31	0	0
Total	204	0	0

1939 interval The mortality rate varied from 0.53 per cent in the simple acute variety to 11.2 per cent in the perforated appendix showing peritonitis, with a total mortality of 2.7 per cent

Sulfanilamide was applied intra-abdominally in nearly all the patients during 1940 in whom there was real or doubtful involvement of the peritoneum by infection. Complications seemed less frequent and were less severe, the drug in the dosages used had no severe toxic effects generally and failed to show any destruction of tissues locally. The only local effect noticeable was the encouraging rapidity of healing.

In conclusion we wish wholeheartedly to endorse the use of sulfanilamide intra-abdominally when indicated. We do not desire to give the impression that the mortality rate from the disease with its use will henceforth approximate zero, as we feel unusually fortu-

nate in that there were no deaths from embolism or other conditions entirely dissociated from peritonitis. It is our firm conviction, however, that the dramatic reduction in our mortality rate during the year of 1940 was directly due to sulfanilamide.

## BIBLIOGRAPHY

1. BARROW, W., and OCHSNER, A. Treatment of appendiceal peritonitis. *J Am M Ass*, 1940, 115: 1246-1249.
2. DAVIS, H. H., and McLAUCHLIN, C. W., JR. Results of treatment in acute appendicitis. *Surg, Gynec & Obst.*, 1940, 70: 713-715.
3. DRAPER, JOHN W., and KAUER, JOSEPH. By personal communication.
4. GARLOCK, J. H. Incisional hernia following operation for acute appendicitis. *Surg Clin N America*, 1939, 19: 449-452.
5. HORSLEY, J. S., JR. Abstract of discussion. *J Am M Ass*, 1940, 115: 1250.
6. LADD, W. E. Immediate or deferred surgery for general peritonitis associated with appendicitis in children. *New England J Med*, 1938, 219: 329.
7. MILLER, FELL, BROCH, and TODD. Acute appendicitis in children. *J Am M Ass*, 1940, 115: 1239-1242.
8. REID and MONTANUS. Appendicitis, analysis of 1153 cases at Cincinnati General Hospital. *J Am M Ass*, 1940, 114: 307-311.
9. STAFFORD, F. S., and SPRONG, D. H., JR. The mortality from acute appendicitis in the Johns Hopkins Hospital. *J Am M Ass*, 1940, 115: 1242-1245.
10. WINTHROP CHEMICAL Co. By personal communication.

# THE NEUROGENIC FACTOR IN INTESTINAL OBSTRUCTION

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THE importance of afferent nerve impulses from obstructed distended intestine is again being stressed. Braun and Borritau were the first to postulate a neurogenic theory for death in obstruction, according to which noxious stimuli reach the brain and produce failure of vasomotor and other centers. Whipple, Stone, and Bernheim observed that the duration of life in their experimentally obstructed dogs was directly proportional to the degree of distention but considered absorption of toxins the cause of death. Dragstedt found that the toxemia was relieved and the chlorides rose in the blood when the obstructed loop was aspirated through the abdominal wall. He considered distention merely an accessory factor which damaged the intestinal mucosa permitting bacterial toxins to be absorbed. Burget et al. noted that a sick dog refusing all food would often eat eagerly 30 minutes after an obstructed loop was aspirated. He decided that death is due to loss of chlorides in the vomitus and that the vomiting is due to reflex nausea and pain from the distended loop rather than to absorption of toxins. Herrin and Meek (10) placed balloons in Thirty Vella loops. The balloons were maintained at a constant pressure of 50 to 80 millimeters of mercury. Fourteen dogs thus treated died in 8 days. The symptoms and blood changes were those of acute intestinal obstruction. Herrin and Meek pointed out that the beneficial effect of saline injections, re introduction of vomitus and aspiration of closed loops might all be explained by dilution, neutralization, or withdrawal of toxin. The authors thus disposed of the toxin theory since death occurred despite free drainage of Thirty Vella loops. By administering 30 cubic centimeters of 10 per cent sodium chloride daily these workers kept a dog alive for two

14-day periods of distention. A third period of distention without salt resulted in the death of the dog. Meek and Herrin then denervated similar draining loops. Of 8 animals thus prepared 3 endured the distention for 20, 21 and 23 days, respectively with no symptoms and normal blood chemistry. Four others showed "undoubted protection. They concluded that distention causes reflex vomiting and inhibition of appetite and as a result death occurs from unbalanced chloride loss.

Ender and Herrin divided the jejunum 25 centimeters from the ligament of Treitz, inverted both ends, and anastomosed the distal end to the stomach or duodenum, thus producing complete simple obstruction of the jejunum. The fluid from the obstructed bowel returned to normal bowel so that there was only slight loss from vomiting. Four dogs lived 8 days (perforated) 2, 4 and 6 weeks, respectively. Of two denervated animals, one was without symptoms for 16 days and then died on the seventeenth day within a few hours of the onset of symptoms. The other dog was reported normal on the eighteenth day of obstruction. Since all dogs survived far beyond the 8 days (except the one with perforation) reported for simple jejunal obstruction, the authors concluded that the rôle of toxemia in acute obstruction seems to be of less importance than chemical or nervous factors.

Taylor, Weld and Harrison introduced a balloon into the duodenojejunum with a by pass of heavy walled rubber tubing. In this manner the authors were able to distend the intestine with pressures of 60 to 110 millimeters of mercury without completely blocking the lumen. They showed fluoroscopically that a barium meal passed through the rigid tube beside the distended balloon. Dogs thus prepared vomited only occasionally the blood chlorides remaining near normal yet all died within 54 hours. However if the segment of

bowel holding the balloon was denervated, the dogs survived the distention about 72 hours, dying of peritonitis induced by balloon erosion of the gut. Taylor and his co-workers believe distention per se is the primary cause of death in intestinal obstruction, i.e., afferent nerve impulses from the distended viscus cause the vomiting, fall in pressure, and collapse of acute intestinal obstruction.

Best and Taylor stress that acute distention of even a small intestinal pocket as in Richter's hernia in which the intestinal lumen is not entirely occluded, leads to all the symptoms of intestinal obstruction. Wangenstein and Rea by excluding swallowed air (cervical esophagostomy) and preventing distention in dogs with complete occlusion of the terminal ileum spared these animals for an average of 36 days (giving 1500 cubic centimeters of 1 per cent saline daily and occasional blood transfusions). These authors concluded that the mechanical factor of distention and not a toxic factor accounts for the lethal issue in ileal obstruction.

Finch, Rosenfeld, and Gendel resected the celiac ganglion and all the splanchnic nerves (and/or the subdiaphragmatic vagus nerves) in cats, checking the completeness of the denervation at autopsy on the death of the animals. They concluded that exclusion of the extrinsic nerve supply does not influence the survival time. However, Herrin and Meek (11) found vagotomy, splanchnicotomy, and lumbar sympathectomy permitted the distention of Thiry-Vella jejunal fistulas without any symptoms in 6 dogs. Bilateral splanchnicotomy and lumbar sympathectomy prevented vomiting and to some extent the depression, but anorexia appeared.

Our observations indicate that denervation does exert a protective effect and by using non-draining loops distended by the gas and secretion resulting from the obstruction alone, we produced the ideal medium for absorption of any specific toxin formed in intestinal obstruction.

#### METHODS

Obstruction of the first portion of the jejunum, 15 centimeters from the ligament of Treitz, was produced by the technique of

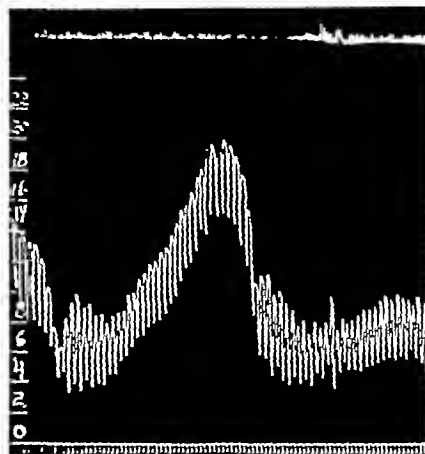


Fig 1 Tracing of denervated non draining jejunal loop, obstructed for 12 hours. Top tracing, respirations, timer, 4 second intervals, scale, pressure in centimeters of water.

Stone, Bernheim, and Whipple, i.e., resection of a 10 to 12 centimeter segment, inversion of the ends to form a closed loop, and then re-establishing the continuity of the gastrointestinal tract by an end-to-end anastomosis. Numerous workers have shown (6, 5, 13) that death occurs more rapidly under these conditions than if the bowel is obstructed by a single ligature at this level. Denervation of these obstructed loops was effected by dissecting out the central vessels, cutting all other structures and painting the vessels with 20 per cent phenol in 15 dogs. Denervation was produced in 6 dogs by infiltrating the mesenteric pedicle with 95 per cent alcohol (or ether, 2 dogs).

In 6 dogs the motility of the obstructed denervated loops was studied by inserting balloons connected to water manometers and recording tracings of pressure changes on smoked paper. These observations were made on unanesthetized animals at variable intervals of obstruction.

Animals were operated upon under intraperitoneal sodium pentobarbital anesthesia. No special postoperative care was given. Water was placed in the cages next day and the stock diet the following day.

#### RESULTS

In the 6 dogs prepared for motility studies of denervated obstructed loops, the average of the maximum spontaneous pressures is 27

centimeters of water which is not significantly different from the average (26.8 cm.) of non-denervated obstructed loops (1). Our observations show that the motility pattern of denervated obstructed intestine is similar to non-denervated obstructed intestine. Denervation, then, does not interfere with the building of increased pressures in obstructed loops (Fig. 1).

Of 10 non-denervated control animals, all died in 36 hours to 7 days, the median being approximately 72 hours. At autopsy 7 loops were perforated and 3 were distended. Of 13 denervated dogs 11 lived and 2 died (3 to 4 days). At autopsy in the animals which died every loop (but one) was perforated and death was attributed to peritonitis.

The dogs protected by denervation lived from 3 weeks to 4 months. Five dogs were killed when normal for 4 to 8 weeks. These animals did not vomit after the first day or two ate voraciously were active and alert. When killed, the examination revealed that 3 dogs had collapsed loops containing 10 to 20 cubic centimeters of gray mucus fluid while two had markedly distended loops, a culture from one yielding a pure growth of streptococci (hemolytic and non hemolytic). The contents of these loops was fecal in character with very foul odor. Six animals died in from 3 weeks to 4 months. These were entirely normal until 1 to 2 days before death when they became listless, vomited and refused to eat. Four dogs dead of internal herniation and volvulus apparently had acute accidents avoidable with better surgical technique. Why two animals should suddenly develop generalized gas gangrene after 3 and 4 months of normal livelihood is not apparent. It is conceivable that the anaerobic bacteria finally got a foothold and produced active infection. These dogs were tremendously distended and solid organs, like liver and spleen, were crepitant and literally bubbling with the gas.

#### EVALUATION

Denervation of an obstructed non-draining loop of intestine apparently will protect a dog against death for 3 or 4 months if the loop does not perforate. If perforation occurs the animal dies of peritonitis. It is not apparent

why some loops perforate while others with stand marked distention for long periods. It was noted in the non-denervated controls that 3 of the dogs died with distended non-perforated loops. It is well known that death frequently occurs from distended discolored bowel which has not perforated. It has been shown (9) that death in closed loops, even when strangulated, can occur without bacteria in the peritoneum or the blood stream.

Herrin and Meek (10) have not disposed of the toxin theory by draining the loops to the outside since the toxin is believed by advocates of the toxin theory to be formed in the mucosa and absorbed under the influence of the distention directly into the veins and lymphatics. Our closed loops should be ideal for absorption of toxins under the pressure produced by the obstruction itself but dogs with denervated loops lived unless the loops perforated. That denervation eliminates a neurotoxin is unlikely since animals dying of closed loop obstruction do not die of progressive paralysis; also several animals were saved with nerves spared but rendered nonconductive by ether or alcohol. That elimination of lymphatics is a protective factor is not probable since these are quickly reformed.

The data show that the protective effect of denervation is not due to altered motility.

#### SUMMARY

1. Dogs were prepared with closed loop obstructions, 10 serving as controls while 13 were denervated.

2. Balloon studies of intestinal motility were done in 6 unanesthetized dogs with denervated closed loop obstructions.

3. Denervation does not significantly alter the motility of obstructed loops.

4. Denervation of an obstructed non-draining jejunal loop prolongs life, dogs dying after 3 or 4 months of generalized gas gangrene. There is, therefore, no evidence for the existence of a special toxin of intestinal obstruction.

#### REFERENCES

- ANTONIC, R. F., and LAWSON, HAMPHREY. The muscular activity of the small intestine in the dog during acute obstruction. *Ann. Surg.* (in press).
- BLAIR, C. H. and T. YLON, N. B. *Physiological Basis of Medical Practice*. Baltimore: Williams Wood & Co. 937.

- 3 BRAUN, W, and BORRUTAU, H    Experimental kritische untersuchungen ueber den ileustod    Deutsche Ztschr f Chir, 1908, 96 544
- 4 BURGET, G Z, MARTZLOFF, K, SUCKOW, G, and THORNTON, R C B    Intra-loop pressure and clinical condition of animal    Arch Surg, 1930, 21 829
- 5 COPHER, G H, and BROOKS, B    Intestinal obstruction, an experimental study of the therapeutic value of sodium chloride    Ann Surg, 1923, 78 755
- 6 DRAGSTEDT, L R    Blood chemistry in intestinal obstruction    Proc Soc Exper Biol & Med, 1928, 25 239
- 7 ENDER, C A, and HERRIN, R C    The relative importance of toxemia in jejunal obstruction in dogs    Am J Physiol, 1939, 126 485
- 8 FINE, JACOB, ROSENFELD, LOUIS, and GENDEL, SAMUEL.    The rôle of the nervous system in acute intestinal obstruction    Ann Surg, 1939, 110 111
- 9 HARTWELL, J A, HOGUET, J P, and BEEKMAN, F    An experimental study of intestinal obstruction    Arch Int Med, 1914, 13 701
- 10 HERRIN, R C, and MEEK, W J    Distention as a factor in acute intestinal obstruction    Arch. Int. Med, 1933, 51 152
- 11 Idem    Afferent nerves excited by the distention of the jejunum in dogs    Am J Physiol, 1939, 126 532
- 12 STONE, H B, BERNHEIM, B M, and WHIPPLE, G K    Intestinal obstruction, an investigative study of the toxic factors    Bull Johns Hopkins Hosp, 1912, 23 159
- 13 SWEET, J E, PEET, M M, and HENDRIX, B M    High intestinal stasis    Ann Surg, 1916, 63 720
- 14 TAYLOR, N B, WELD, C B, and HARRISON, K    Experimental intestinal obstruction    Canad M A J, 1933, 29 227
- 15 WANGENSTEEN, OWEN H, and REA, CHARLES E    The distention factor in simple intestinal obstruction    Surgery, 1939, 5 327
- 16 WHIPPLE, G K, STONE, H B, and BERNHEIM, B M    Intestinal obstruction    J Exper Med, 1913, 17 286



# FAT EMBOLISM

## A Clinical and Experimental Study

CARLO S. SCUDERI M.D. Ph.D. F.A.C.S., Chicago, Illinois

SINCE over 600 known references to fat embolism are found in the literature only the high lights of the literature that pertain to the experimental and clinical work to follow will be presented. Clinically fat embolism is very difficult to substantiate conclusively. This difficulty is really not the fault of the medical profession but is due to the nature of the disease, which makes its incontestable recognition very problematic. For this reason I have spent most of my study on the diagnostic phase of this malady. Those desiring complete reviews on the subject should refer to articles by Warthin 1913 Scuderi (42) 1934 and Groszkoss, 1936

### HISTORICAL

As early as 1669 Lower had injected milk intravenously in dogs, and this was probably the beginning of our knowledge of fat embolism.

Magendie during the years 1821 and 1836 did some experimental work on Epimeria and its effect on the circulation in animals. His description of the experimental introduction of liquid oil into the venous circulation is classic.

Zenker 1862 observed the first fat emboli in the pulmonary capillaries of man following a severe crushing injury to a railroad worker. The pulmonary capillaries were found to contain a great many emboli of fluid fat. He thought that they occurred by aspiration through the gaping veins from the stomach of the patient.

Scriba in 1880, reviewed all the cases up to date and then added 34 cases of his own. He also conducted animal experiments and brought forth many clinical and pathological points which had previously been obscure. Most of our modern textbooks dealing with the subject of fat embolism are based upon

the statements and conclusions which he drew. However years have shown that some of his opinions were erroneous. Of 177 cases of fat embolism which he collected in only 14 instances could fat embolism be regarded as the cause of death, and some of these he regarded as doubtful.

Lehman and Moore (1927) by *in vitro* experiments showed that histamine extracted from necrotic muscles, produced a very rapid disintegration of the fat emulsion of normal blood serum. They concluded that fat embolism might be readily produced in the bone marrow on a non-traumatic basis purely by the absorption of histamine from injured body tissue, into the blood stream. They also found that intravenous ether produces fat embolism of the lung by dissolving the normal emulsified fat of the lungs, and, when the ether vapor tension is lowered by evaporation into the alveoli, the free fat becomes visible microscopically in the blood.

### ETIOLOGY

The experimental work done on the etiology of fat embolism has been considerable and, in many instances, has led to much contradiction and confusion.

Males are many more times affected than females, the proportion being about 8 to 1. The youngest case on record, a newborn, was reported by Nicod. The greatest incidence is during the fourth decade of life. Rarely does fat embolism occur in children because the fat in the bone marrow is insufficient up to the fourteenth year (Speed). Landois, in an excellent article on the subject, states that he found mostly palmitin and stearin in children and infants, with a smaller proportion of the more fluid olein. At body temperature oleic acid is quite fluid and is more easily absorbed than the more viscous palmitic and stearic acids. For this reason fat embolism is not so common in children.

It appears as though alcoholics are more predisposed than nonalcoholics. Perhaps this is due to the instability of the fat emulsion in the serum produced by the frequent dilution with the fatty solvent after a "debauche" (Cubbins).

Lehman and Moore calculated the amount of fat in the bone marrow of a femur and found it to be approximately 65 cubic centimeters. By experimental study with cottonseed oil they found that, should man be able to tolerate as much oil in the blood stream as a dog, 120 cubic centimeters would be required for a lethal outcome. This is based on two assumptions: first, that cottonseed oil does not materially differ from bone marrow fat, and, second, that man, as well as dogs, can tolerate free fat in the blood. If this be true, all the fat in the bone marrow of a femur could be well tolerated. After a great deal of controversy as to whether the fat is carried by the blood or lymph vessels, the present opinion seems to be that most of it is carried by the veins while a smaller part may be carried by the lymphatics.

It is interesting to note that experimental animals can be made to build up a resistance to experimental fat embolism by repeated small injections of fat. This work was done primarily by Paul and Windholz, and later by Domanig. They found that such animals could withstand many times the lethal dose. No fat droplets could be found free in the blood serum of these animals. Evidently they are rapidly destroyed by a newly formed, unknown substance.

#### PATHOGENESIS AND PATHOLOGY

After the injury to the bone marrow fat or adipose tissue, there is a disintegration of the supporting fibrous tissue with liberation of the fat. Naturally there are ruptured blood vessels in the vicinity of the injury. The arteries squirt more blood into the area, thereby increasing the pressure, while the veins remain open and absorb the fatty mixture by venous suction (Miloslavich), particularly if their consistency is more or less fluid.

Gauss (20) brings out the point that fat embolism is more common in fractures than in any other condition because the veins are

encased in a bony wall and hence cannot collapse as elsewhere in the body, thus they remain wide open for the admittance of the fatty mixture. This process may take place immediately or proceed for some time until coagulation occurs. The pathology of this condition involves all the organs and is too well known by all to be discussed in this very brief résumé.

Lehman and McNattin found at postmortem examination that fat embolism is present in the lungs of about 50 per cent of unselected cases. These men have conclusively shown that anatomically the diagnosis of fat embolism as the cause of death cannot be safely made.

Wright found at postmortem examination fat embolism present in 52 of 100 consecutive cases, in the majority of which patients did not suffer from fractures or contusions from falls or accidents. This author also helps to substantiate the contention that postmortem findings of fat embolism are not pathognomonic evidence of violence.

Carrara found fat embolism present in 22 per cent of cardiovascular renal diseases and 44 per cent of burns. Catsaras reported fat embolism in the lungs of 18 of 67 cases of post-influenzal pneumonia. To add to the already great confusion on the subject, acidosis, phlegmonous gastritis, acute pancreatitis, chronic tuberculosis, menstrual suppression, hepatitis, splenitis, and tuberculous pneumonia have been mentioned. In fact, almost all diseases, poisonings, and injections to which the body has been subjected have been reported in the literature as having caused fat embolism at one time or another.

Vance, in 1931, wrote a very comprehensive paper on fat embolism from a pathological viewpoint, which is a classic on the present literature on the subject.

#### SYMPTOMS

There is no clinical correspondence between the apparent injury and the degree of resulting lipemia. Injuries which are apparently identical may in one individual be followed by a fatal lipemia, while in another individual the same injuries may cause but a slight disturbance.

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From the University of Illinois, College of Medicine.

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#### SYMPTOMS

There is no clinical correspondence between the apparent injury and the degree of resulting lipemia. Injuries which are apparently identical may in one individual be followed by a fatal lipemia, while in another individual the same injuries may cause but a slight disturbance.

The onset may be sudden within a few hours of the injury but usually does not become manifest until the third or fourth day. Once the symptoms set in, they may vary from a slight irritability and excitability of the patient to maniacal periods associated with high grade delirium and death. The symptoms, if watched carefully, have a tendency to be cyclic, corresponding to the emboli passing from the pulmonary circulation to the systemic, and gradually returning. Many of these cases appear to be doing nicely when gradually they begin to show some signs of nervousness and excitability. At this time the pulse and temperature begin to show a slight rise. The respirations show a more rapid rise than the pulse, and even early in the symptomatology may be dyspneic. As more capillaries are obstructed in the lungs, the dyspnea increases correspondingly. Cyanosis may or may not appear depending on the extent of pulmonary impairment. Gradually a passive congestion occurs in the lungs and moist rales are audible over the bases. A cough begins to appear and is of a productive nature rarely blood-stained however. For this reason, many such cases are diagnosed as bronchopneumonia.

As the pulmonary arterial pressure increases the heart must beat faster in order to overcome the circulatory resistance. The pulse becomes faster and stronger and the blood pressure begins to rise. Should the resistance in the pulmonary circulation increase or remain great, the heart before long begins to weaken. Its rate increases while its force decreases. The blood pressure correspondingly begins to fall. Should some of the emboli lodge in the coronary vessels, then the cardiac failure comes on much more quickly. Before long the pulse becomes imperceptible, the arterial pressure falls, the venous pressure rises and the picture of deep shock and cardiac failure appears.

The temperature varies from subnormal to 106 to 107 degrees F., depending on whether or not the heat regulating center is disturbed by the emboli. The usual temperature during the height of the disease, is about 103 degrees. In terminal cases the temperature often rises much higher.

Petechial hemorrhages (Ryerson in 1916) may appear in the skin as in any other disease in which the embolic phenomena predominate. However, due to the fact that the capillaries are not actually occluded as in bacterial endocarditis but the circulation is greatly slowed down because of the increased viscosity of the blood (Gause, 19) they are rare. LeCount and Gause published the results in 14 cases of death following fat embolism upon which postmortem examinations had been done. A study of the clinical symptoms of these cases is very instructive as it gives us some idea of what occurs in milder cases which do not have an *exitus letalis*.

All of these patients passed from consciousness to a restless stage. In 12 this took the form of delirium, 11 becoming so violent as to require restraint. Eleven passed from delirium to the comatose state. In all 14 cases dyspnea was present, and also an associated increase in respiratory rate, the average being 53 respirations per minute. Two cases developed Cheyne Stokes respiration. 4 suffered from air hunger. 3 developed a marked cough. The pulse became weak and shallow and averaged 153 per minute. Involuntary passage of urine and feces occurred in 12 and in the 2 others the records were incomplete. At the time of admission the temperature was either normal or subnormal and then rose to an average of 105.2 degrees F. for the 14 cases. The time that they lived varied from 2 to 17 days, with an average of 6 days.

#### DIAGNOSIS

The majority of cases of fat embolism are so mild that they do not cause symptoms, or so severe that death results in a few days from involvement of the lungs or the brain. During life the diagnosis of fat embolism is justified only if there is a history of an injury with the typical clinical manifestations.

The incubation period varies from a few hours from the time of accident to 3 or 4 days. It is a good point to remember Dennis' rule in this respect, regardless of the exceptions: shock 3 hours, fat embolism, 3 days, pulmonary embolism, 3 weeks (Speed).

Additional confirmatory signs are the presence of fat in the urine, the demonstration of

## SCUDERI FAT EMBOLISM

fat emboli in the retinal vessels by the ophthalmoscope, and the appearance of petechial hemorrhages in the chest, shoulders, and neck. The presence of the large circular cells of Liting and Martin or the fat globules of Warthin and Martin are not pathognomonic signs, as they are found in conditions other than fat embolism. As a rule, fat embolism is rarely diagnosed from clinical signs and symptoms, it is most often discovered accidentally at necropsy.

In the differential diagnosis delirium tremens, skull fractures, bronchopneumonia, and shock must be most seriously considered.

### PROGNOSIS

The prognosis in fat embolism should always be reserved because some of the patients who appear to be coming along well suddenly grow worse and die. As to life, most of the patients recover, but due to the fact that only the fatal or very sick cases are diagnosed and the mild cases overlooked, most people have the reverse idea.

### TREATMENT

As fat embolism in fractures is not of common occurrence, and when it does occur is rarely diagnosed, one can understand why reports regarding the treatment of this complication are not very illuminating. Grondahl states that a terminal result occurs in but 1 of every 3,000 cases of fracture, and that death attributed to fat embolism in fracture cases occurs in only 1 per cent of the cases.

Much experimental work has been done on the prophylaxis, with much forethought and logical thinking. Wells, Ryerson, and Caldwell and Huber have shown that a tourniquet, if used during the operation or manipulation, reduces the possibility to a minimum, especially if it is allowed to remain in place for an hour after the operation. Simonds found that etherized dogs were more susceptible to fat embolism than were those anesthetized by non fat solvents. This is a point of some importance and if another anesthetic which is not a fat solvent can be used as efficiently and safely it should be given preference.

Warthin advises the following prophylactic management: 1. Avoidance of unnecessary or

rough handling of patients 2. Immediate splinting and early reduction of all fractures (Tanton) 3. In orthopedic operations use of a saw in preference to the chisel, if possible (Lever) 4. Slow removal of Esmarch's bandage (Buerger, Aberle)

Reimer advises canaliculizing the vein, allowing the first blood after removal of the constrictor to flow out. Czerny, and 50 years later Wegelin, also advocated the injection of sodium carbonate, probably with the idea of forming a soluble soap. This method has fortunately received but little support. All experimental animals died under this regimen.

The active treatment of this condition is very poor, and many of the suggested methods are not only theoretically, but also practically, in error.

Czerny advises venesection to lessen the venous congestion. Schanz believes physiological salt solution both intravenously and by hypodermoclysis to be of benefit, while Bissell believes that such a procedure is contra-indicated because of increased pressure to the right heart.

Wilms suggested drainage of the thoracic duct. Fritsche found experimentally that if this was done at the first appearance of the symptoms it helped. Grondahl found that even ligation of the femoral vein and removal of the inguinal glands did not prevent fat embolism.

Wilms also advised incising the area of fracture and combating its origin by evacuating the blood and fat.

Pituitrin, pituglandol, caffeine, coranin, morphine, and sympatol have been suggested in the active treatment as they have been found both experimentally and clinically to produce a steady fall of blood fat.

### VALUE OF BLOOD CHEMISTRY AND PHYSICAL MEANS OF QUANTITATIVE BLOOD FAT DETERMINATION

Since the problem of fat embolism has to do with the presence of fat droplets in the blood stream, it was thought that quantitative blood fat determinations would be of material aid in its diagnosis. For this reason the known methods were looked up and studied in great detail.

Kumagawa and Suto described a saponification method in 1908. Bang in 1918 described an extraction method, which however is not accurate enough for a truly scientific method. Bloor, Pelkan and Allen (6) first brought the nephelometric method to the foreground in 1922. Later in 1928 Bloor (5) published an improved method. Stoddard and Drury described a titration method in 1929.

After a careful study, counsel was sought from several very well known physiological chemists and all agreed that the methods were beyond the capacity (or ability) of the average part-time chemist, and even when the determinations were done in well equipped laboratories by properly trained men, the variations were too great to be of real diagnostic value. For the present at least, the outlook along these lines is unfavorable.

Clinical investigation in the serological department of the Cook County Hospital has revealed many blood serums of almost cream-like appearance. These were found in diabetic comas, lipid nephrosis, and lactating postpartum women. In spite of the fat content of the blood having reached this startling height, these cases revealed no manifestations of fat embolism. Some investigators have found diabetic coma cases to have reached a concentration of total lipoids in the blood of 26 per cent (Bantlin) compared with the normal of 0.4 per cent. These observations, therefore, have conclusively proved to the author that it is not the total fat content of the blood which we should be interested in, but the state in which this fat is found. Should it be in the form of a stable emulsion, no fat droplets are present in the blood, hence no embolism can occur. On the other hand, the corpuscular fat content is of all importance as it causes the occlusion of the vessels giving the embolic phenomena. Unfortunately only 5 per cent of the total fat content of the blood is found in this form. If one considers that the total fat content, as has been stated before is only 0.4 per cent, the figure of the corpuscular percentage almost approximates zero. Therefore it stands to reason that any total chemical method for determining increases or decreases of this element would be far beyond the scope of quantitative chemical determinations as the

percentage of error by our best present day methods would be too great.

Other fields of experimental work were searched for possible aid in these determinations. The use of the spectroscope was suggested. However it has been stated that the fat concentration was too small to produce any appreciable variations.

At a later date the possibility of the use of electroconductivity to determine fat content changes in blood serum was considered but this method and also the use of the polariscope has been found to be of negative value and henceforth dropped.

#### RESULTS OF DARK FIELD EXAMINATIONS OF THE BLOOD AND FRESH SMEARS OF RECENT FRACTURES AND CONTROL CASES

Edmunds first described the dark field examination of the blood for fat particles in 1877. Further work along these lines was carried on by Neumann in 1907. Gage and Fish (18) in 1924 published a most excellent article upon this subject, on investigative work on fat absorption and metabolism in the lower animals. Gage (17) was the first to give these microscopic particles the name of chylomicrons, 1930 meaning that they are one micron in diameter and are composed of chyle.

The study of 25 miscellaneous blood serums from the medical wards of the Cook County Hospital, was undertaken as a control study. No variations from the normal were found. Several cream like blood specimens from a lactating postpartum woman revealed a few interesting observations. In spite of a cholesterol of 335 milligrams, and a milky appearing serum, no actual fat droplets could be found, a fact showing the marvelous stability of a serum fat emulsion.

As the average blood cell is 10 microns in diameter it has been estimated that in order to occlude the finer capillaries of the lung the fat droplet must be at least 12 to 15 microns in diameter. In none of the control cases was this found.

In order to show the feasibility of this diagnostic method in embolic cases, olive oil was injected intravenously in a dog. Five cubic centimeters were used, and it was injected slowly. Two minutes later with a clean

# SCUDERI FAT EMBOLISM

syringe and needle, 1 cubic centimeter of blood was removed from the opposite leg, and a drop was examined under the dark field. Large ameba-shaped droplets of olive oil could be easily demonstrated, at least twice the diameter of an erythrocyte.

Twenty-five fresh fracture cases from the service of Dr William R. Cubbins were now selected. All were suffering from major fractures from 3 to 144 hours from the time of accident. One whole blood and one centrifuged serum specimen of each patient was examined. No difference was found between the specimens except that the centrifuged serum was easier to examine due to the lack of interference of a large number of blood cells.

No actual fat droplets were found. I am of the opinion that patients suffering from true fat embolism will show droplets in great number, and that this method will be of a real diagnostic aid.

## TECHNIQUE OF URINE ANALYSIS IN FAT EMBOLISM

In the study of this problem, several hundred urine specimens have been examined for the presence of fat in the urine of suspected cases. After a period of time, it was found that this apparently simple investigative phase of the problem offered an interesting physical phenomenon which heretofore has evidently not been emphasized, and for this reason I undertook its investigation.

That fat is excreted by the kidneys into the urine in cases suffering from fat embolism is well known and often spoken of in the literature. Unfortunately, however, its detection is difficult because of one very elementary physical phenomenon, and that is that the fat droplets float on the surface of the urine, and therefore are not excreted from the bladder unless the last few cubic centimeters of urine are expressed. For this reason many urine examined which contain fat are negative because of this simple oversight.

To prove conclusively this contention, two flasks were used to carry out this experiment *in vitro*. The setup used is illustrated in Figure 1. The flask above represents the kidney, the one below, the bladder. These are

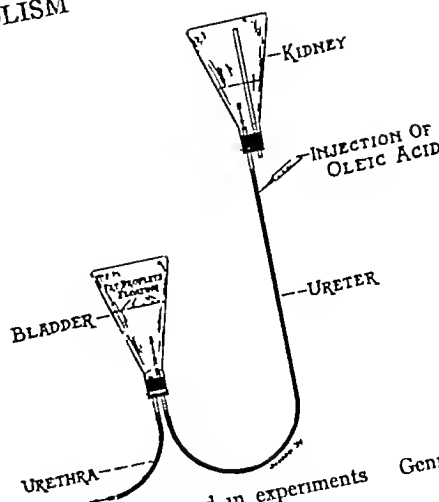


Fig 1 Set up used in experiments Genito-urinary system *in vitro*

connected by a rubber tube representing the ureter. A second tube from the lower flask represents the urethra. The fluid was permitted to run very slowly from the top flask to the lower, and fine droplets of oleic acid and also olive oil were injected into the tube close to the top flask with a hypodermic syringe. In this manner there existed a visual genito-urinary system. It was noticed that as the fluid accumulated in the lower flask, the fat droplets rose to the top. (In both the *in vitro* and clinical experiments 2 cubic centimeters of oleic acid were used, divided into small droplets by simple shaking with water.)

After the lower flask was filled, the pinch clamp on the rubber tube representing the urethra was removed, and the fluid permitted to flow out. The entire contents of the flask, with the exception of the last few cubic centimeters of fluid, were absolutely fat free. Both urine and plain tap water were used as the fluid in the *in vitro* experiment, and the physical phenomenon was found to be the same.

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Two to 3 hours after the fat injection in the pelvis of the kidney, the males were



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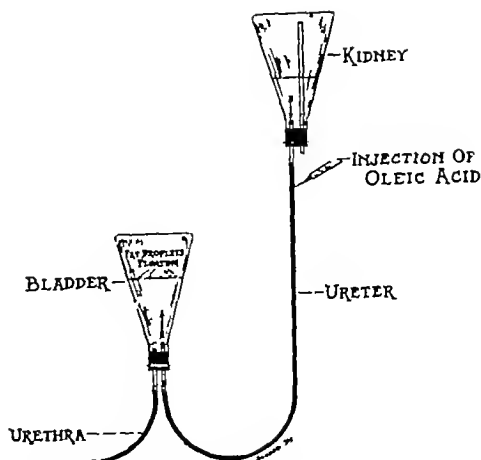


Fig. 1. Set-up used in experiments. Genito-urinary system *in vitro*.

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Two to 3 hours after the fat injection into the pelvis of the kidney, the males were in-

TABLE I.

Type of fracture	Number of hours since accident	
Tibia	30	24
Femur	4	24-48
Humerus	7	48-72
Ulna	1	72-96
Patella		96-120
Forearm both bones		90-144
Pelvis		144-68
Ribs		Total cases
Total cases	50	50

Number of cases showing fat	Number of cases showing urine casts
Urine	9 cases from
Blood serum	L.P.F. in centrifuged specimens

structed to pass the urine into 5 to 7 flasks, urinating not more than two fingers' depth in each. In both cases, the last flask contained all of the oleic acid while the others were absolutely fat free. Due to the difficulty of collecting the divided urine specimens in the female they were catheterized with glass catheters. In both cases the urine flow ceased without evidence of any fat floating in the flasks, but when the patient was compelled to sit up then the oleic acid filled the glass catheter and not another drop of urine was expressible.

#### A CONTROL STUDY OF THE URINE AND BLOOD EXAMINATION IN NON-EMBOLIC CASES

As far as one is able to determine from the literature the study of the urine and blood serum in normal cases and fresh fractures has never been done. For this reason the following work has been carried on to see whether or not free fat is found in normal control cases.

Two hundred miscellaneous hospital cases were used for the urine examination. In this series only ambulatory male patients were used because of the greater ease in collecting the urine specimen. Great care was exercised in this work to have the patient empty his bladder completely. Unless all of the urine of the bladder is collected, the floating fat droplets will not be expelled, and hence the urine examination would convey the wrong conclusion.

The urine specimens were collected and placed in a cold place overnight. The next morning the surface of the urine would be carefully examined for floating fat droplets.

Any questionable droplets were removed, stained with Sudan III and examined microscopically. In this entire series not one case showed any free fat.

The serology department of the Cook County Hospital was kind enough to permit the unlimited use of the blood serums sent to them for Wassermann tests. Each specimen was labeled, centrifuged and then placed in the refrigerator overnight. The following morning each tube was carefully examined. All questionable droplets or debris were stained and examined microscopically. On 5 occasions definite fat droplets were found floating on the surface. However the findings proved only that the needles had been kept in liquid petrolatum in each case and evidently the boiling did not dislodge the oil from the inside of the needle but when the blood was drawn for examination the oil found its way into the specimen.

Eleven of these cases showed a chylous emulsion which rapidly found its way to the surface. This is physiological, as any blood serum drawn within an hour or two after the ingestion of any fatty material presents this phenomenon. In each of the cases cited here in the contention mentioned was found to be correct.

Fifty fresh fracture cases were next studied. Only male patients suffering from major fractures were examined. The duration of the fractures was from 1 to 7 days. The urine was collected by having the patient in either the sitting or standing position and then having him completely evacuate the bladder. Ten cubic centimeters of blood were then drawn from the arm and both specimens were centrifuged and examined. The urine residue was stained with Sudan III and examined microscopically. Occasionally casts were found but in not one instance could fatty casts be found as Riedel described as being present in the urine of 42 per cent of cases with fresh fractures.

The casts were no more numerous nor in any way different from the casts found in any group of urine specimens. Not one specimen of blood serum or urine showed any evidence of free fat droplets. A résumé of these cases is given in Table I.

## FAT EMBOLISM

THE VALUE OF CHEST PLATES IN ITS DIAGNOSIS  
AN EXPERIMENTAL STUDY

Jirka and Scuderi in 1936 showed for the first time the value of chest plates in the diagnosis of fat embolism

Eleven dogs were used in the experiments, selecting whenever possible an animal weighing close to 12.5 kilograms. Sterile oleic acid was given intravenously to 6, and sterile olive oil to 5 of the animals. Varying doses were used in each experiment.

Due to the research of Landois, who found that olein was the largest component of bone marrow fat, it was decided to try both oleic acid and olive oil in our experiments. The former, being the acid of the trioleate and easily obtainable, was first used. However, as it is toxic and probably unites with the alkaline radicals in the blood stream to form a soap in the chemical sense of the term, olive oil, which is a neutral oil and non-toxic in smaller quantities, was used as a control. It was found that 0.33 cubic centimeter of oleic acid per kilogram of body weight was sufficient to produce death, while 2.2 cubic centimeters of olive oil per kilogram of body weight were required to produce death in dogs. The physical properties of both were similar in that their viscosities were nearly equal and both produced like droplets when emulsified. First the technique for x-ray films of the chest of a dog had to be worked out. Once the plates began to be uniformly good, the oily substances were injected. By taking films before and after the injections, we were able to compare the lung fields, taken in each instance with the same technique.

Figure 2a shows the normal lung field of one of the animals. The lungs are relatively clear, except for the usual hilus clouding. Figure 2b was taken twenty minutes after the injection of 6 cubic centimeters of sterile oleic acid. The lung fields now appear more or less cloudy, of a diffuse, even nature. No patches or increased opacities are noted. The heart shows no enlargement when measured by the superimposition of the films. The following morning the dog was found dead, *rigor mortis* being present. The thoracic organs were removed and roentgenographed *in toto*. The

lungs showed the lack of air. Gross appearance and cut section simulated liver, or the hepatization found in cases of bilateral pneumonia. Palpation revealed no crepitant areas.

Microscopic sections were made and were examined by Dr. Benjamin Nieman of the pathology department of the Cook County Hospital. He described the lungs as being typical of a drowned animal, due to the marked edema of the epithelial cells lining the alveoli, and the clear serous filled alveoli. With Sudan III stain the fat filled capillaries were readily demonstrated.

Figure 3a is of another animal prior to any experimentation. Twenty-five hours after the injection of 2 cubic centimeters of sterile oleic acid, the second film was exposed, Figure 3b. The animal at that time appeared perfectly well and quite normal in every respect. The identical technique was used in both films. Close examination reveals the same diffuse haziness of both lung fields, as seen in the other set of pictures.

Figure 4a shows the normal lung field of another experimental animal. Ten cubic centimeters of sterile olive oil were injected intravenously and 48 hours later another checkup plate was taken, Figure 4b. The same diffuse cloudiness of both lung fields, so characteristically found in all the experiments, was likewise present. The upper lobes show the pathological condition clearly.

From 2 to 12 cubic centimeters of oleic acid were used in the first 6 animals, while from 2 to 20 cubic centimeters of olive oil were used in the last 5.

The animals receiving less than the lethal doses of oleic acid, 4 cubic centimeters, showed evidence of pulmonary irritation for several days. All of these animals had apparent colds, sniffing and coughing periodically, otherwise they appeared normal.

The animals receiving up to 20 cubic centimeters of sterile olive oil showed no evidence whatsoever of any pulmonary irritation or malaise and had no apparent ill effects from the experiments. One of the animals, after having received 20 cubic centimeters of olive oil, became ataxic and had great difficulty in controlling the extremities, although otherwise it appeared normal. The inebriation

stage lasted about 10 minutes, then he ran around and was normal. This period probably existed while the fat droplets were interfering with the cranial circulation.

One must not lose sight of the fact that fat embolism is not a true embolism in the sense of a permanent occlusion of a vessel, but simply a retardation of the blood flow through a capillary while the oil droplets become elongated and are slowly forced from the arterial to the venous side of the circulation.

#### THE SIZZLE TEST FOR FAT IN THE URINE

Accidentally in using the platinum loop for the taking of microscopic specimens, the author noted that whenever fat droplets were present, a sizzling and popping occurred when the loop was heated over an open flame. When no sizzling and popping occurred, only rarely were fat droplets ever found in the microscopic examinations.

This observation was investigated further in order to determine the accuracy of this method for fat determinations.

One drop of olive oil was thoroughly emulsified into increasing dilutions of water and the sizzle test tried. The test was very definite until the dilution reached 1 drop to 80 cubic centimeters of water after which the sizzling and popping was not constant. This represented a dilution of 1:1400 to 1:1600.

Dilutions of 1 drop in 80 to 120 cubic centimeters gave an occasional pop with a discoloration of the flame. One drop in 120 to 150 cubic centimeters just gave a discoloration of the flame this, of course, was of no value.

A bacteriologist has since informed me that she uses this method for hurriedly finding out whether or not any diphtheria organisms are present in a smear because if they are the heating ignites the fatty capsule producing a characteristic popping. Of course she always checked this observation with a culture.

Normal human and dog urines were tested and found to be approximately the same as the tests run with plain water. When no fat was added, only a yellowish blue discoloration of the flame took place.

This simple test requires no special training, no equipment, and its efficiency makes it almost as accurate as a microscopic examination.

#### THE TECHNIQUE OF SUDAN III STAINING OF URINE AND BLOOD SPECIMENS

The staining of urine and blood specimens with Sudan III for examination turned out to be a stumbling block in many of the observations because a number of the details which were important were not appreciated. Until many control studies were undertaken to determine the exact technique, many experiments had to be repeated. The conclusions were as follows: (1) The stain must be fresh (2) a high concentration of the dye is necessary to stain the fat droplets (3) the stain must be permitted to act on the fat for at least 5 minutes in order to stain it well (4) orange droplets less than 3 to 4 microns in diameter are either contamination or undissolved stain (5) a drop of stain must be added directly to the slide and not to a test tube specimen.

#### GARDINOL AND DECHOLIN SODIUM AS THERAPEUTIC AGENTS

Gardinol (sodium lauryl alcohol sulphate) made by DuPont, is probably one of the most efficient emulsifiers known. A few drops added to an oily mixture produces a very fine and relatively stable emulsion with but little agitation. A study of its value in diagnosis has been described elsewhere.

From previous experiments it was found that 2.2 cubic centimeters of olive oil per kilogram body weight was the minimal lethal dose in dogs. Two animals of about the same size were chosen, weighing 10.1 kilograms and 8.9 kilograms. Both received a lethal dose of intravenous olive oil, 2.2 cubic centimeters per kilogram body weight. Five minutes later when the dogs were very dyspneic, one received 20 cubic centimeters of 2 per cent gardinol and almost immediately the dyspnea subsided but within 10 minutes it had returned to almost the same degree. Twenty cubic centimeters more of 2 per cent gardinol was given but the animal was still very ill. The second animal which had received only the olive oil was in *extremis*. Both were observed for 1 hour the gardinol treated animal being in much better physical condition however it was still very ill. The next morning both were found dead. The un-

treated dog was in *rigor mortis* while the gardinol treated animal was still limp

Postmortem examination of both animals revealed a bloody, frothy exudate in both lungs with patches of massive consolidation, more so in the untreated animal. The kidneys, liver, spleen, and intestine showed diffuse areas of hemorrhagic mottling throughout the organs. Specimens were taken and studied microscopically. Massive occlusion of the vessels with droplets of fat was visible in all the sections.

Six more dogs were injected with 2.2 cubic centimeters of olive oil per kilogram and each received 20 cubic centimeters of 2 per cent gardinol immediately after the olive oil was given, and 10 minutes later. All animals died within 12 hours.

*In vitro*, this quantity of gardinol, if properly mixed with 20 to 30 cubic centimeters of olive oil, would produce a very fine and durable emulsion. There is no doubt in the mind of the author that some reaction occurs in the body to prevent the same mechanism *in vivo*.

Since bile salts are emulsifiers and saponifiers of fat, many experimenters have entertained the idea that the injection of a bile salt, provided that it was not very toxic, should help to break up the occluding fat, thereby clearing the obstructed vessels of the interfering fat droplets. Until the commercial preparation of decholin sodium was offered, the bile salts were too toxic to be of any real value. Decholin sodium (sodium dehydrocholate) has been recommended by Paul deHaen Chemical Company as a therapeutic agent in the treatment of fat embolism. It is made by the addition of sodium hydroxide to dehydrocholic acid. This was first synthesized by Hammerstein in 1881. This preparation is the least toxic of the bile salts. Rapport did some experimental work with it and recommended it most highly both as a therapeutic and diagnostic agent. In repeating his work I have unfortunately been unable to corroborate his findings.

As has been stated elsewhere 2.2 cubic centimeters of olive oil per kilogram body weight is the minimal lethal dose in dogs if given intravenously. Varying doses of decholin sodium were employed before, during, and after

the lethal quantity of olive oil. In no instance were any of the animals saved. As far as the author is concerned, decholin sodium is of no value in the therapy of fat embolism.

#### THE MECHANISM OF FAT EXCRETION THROUGH THE KIDNEYS

The author has been unable to find any reference to previous work done on the mechanism of fat excretion through the kidneys. Numerous cases of chylemia have been reported, but all have been purely clinical in their presentation.

This problem was undertaken because of its relationship to the diagnosis of fat embolism in traumatic cases. Before approaching the problem it was necessary to determine whether or not normal dogs under varied physiological conditions ever excreted fat in the urine.

The urine of two normal dogs was examined and found to be negative for fat by microscopic tests described later. Two dogs which had been given one pint of cream, one 3 and the other 6 hours previous to the urine examination, had no fat in the urine. Two other dogs which were being starved in other experiments also showed negative results. The kidneys of these 6 animals were sectioned and stained with Sudan III. In none was there any evidence of fat droplets in either the glomeruli or tubules.

Knowing that dogs under varied physiological conditions did not excrete fat in the urine, its presence should be considered abnormal.

All the animals in the following experiments were operated upon under nembutal anesthesia.

The pedicle of one kidney was isolated through a loin incision and the renal artery carefully dissected from the surrounding tissues. The ureter was then traced to the bladder and cut free, the end being cannulized with a glass cannula. The cannula was then brought out through the anterior abdominal wall through a stab wound and fixed in place. With a very fine needle the fat was injected into the renal artery. When the injection was completed, the renal artery had to be carefully clamped in the longitudinal axis to pre-

vent loss of blood through the needle hole and still not completely occlude the renal artery. Occlusion of the artery would obviously result in cessation of the urinary flow from the isolated kidney. A miniature paper clip was used for this purpose, having a small spring in it. After the fat had been injected the kidney was placed back in the loin and the wound sutured.

Both dog bone marrow fat and olive oil were used in various physical forms. Olive oil or bone marrow fat was used in some emulsified fat in others. As emulsifiers, plain water with a little soap and also solutions of gardinol were tried. The results were uniformly the same. In order to increase the urinary output, intravenous Ringer's solution from 200 to 300 cubic centimeters with 1 gram of caffeine or 200 to 250 cubic centimeters of 2 per cent urea in physiological salt solution were given intravenously. The urine was collected from the cannula in the anterior abdominal wall and examined by centrifuging it for 15 minutes at high speed then staining the supernatant liquid with Sudan III. A film from the surface of the urine was examined under the microscope for the orange colored spherical droplets of fat. When present these varied in size from 3 to 8 microns in diameter.

Results of experiments on a series of dogs and Louisiana bull frogs showed that the intravascular fat is excreted through the kidneys providing that 0.75 cubic centimeters or more fat per kilogram body weight is injected. The fat is excreted not through the glomeruli but only through the tubules. These experiments have been described by the author in detail in a recent article (43).

#### STUDIES ON THE SURFACE TENSION OF BLOOD SERUM

In the search for methods of accurately diagnosing fat embolism the effect of the fat droplets on the blood serum was studied. It is a well known fact that the mixture of liquids of different specific gravity or the addition of inert particles to a liquid, produces definite changes in the surface tension. With this thought in mind experiments both *in vitro* and *in vivo* were conducted.

In order to eliminate the most common factors that produce errors, the eye glass and the platinum loop of the DuNouy tensiometer were washed first with soap and water followed by ether. They were never used until thoroughly dried.

The average of ten determinations was computed and found to be as follows: Control studies at room temperature—water 85.8 dynes human serum, 90.5 dynes dog serum, 90.4 dynes.

Dogs were subjected to increasing doses of olive oil given intravenously. After a few minutes venous blood was withdrawn from the opposite leg and the blood serum collected by centrifuging the specimen.

Two of the experiments were as follows:

Experiment 6 Normal blood serum reading of this dog was 90.4 dynes. One cubic centimeter of olive oil per kilogram body weight was injected, a total of 6.6 cubic centimeters being used. Reading after olive oil was 90.7 dynes.

Experiment 7 Normal blood serum reading of this dog was 88.5 dynes. One cubic centimeter of olive oil per kilogram body weight was injected, a total of 8.63 cubic centimeters being given. Reading after olive oil was 86.6 dynes.

One cubic centimeter of olive oil per kilogram body weight is about one half the lethal dosage in man a comparable amount would be 70 to 75 cubic centimeters. These two determinations showed but little difference in the readings. Other experiments running up to a lethal dosage (2.2 cubic centimeters of olive oil per kilogram body weight) showed very little change in the surface tension determinations. Probably many of the olive oil droplets were being held back by the small capillaries of the body and for that reason many of the droplets were not to be found in the general blood stream as we had anticipated.

Further studies were made on the variables produced by olive oil in blood serums *in vitro*. The results were as follows: ratio 151 cubic centimeters per 5000 cubic centimeters of blood—(lethal dose in man) 82.75 dynes ratio 224 cubic centimeters per 5000 cubic centimeters of blood—77.75 dynes.

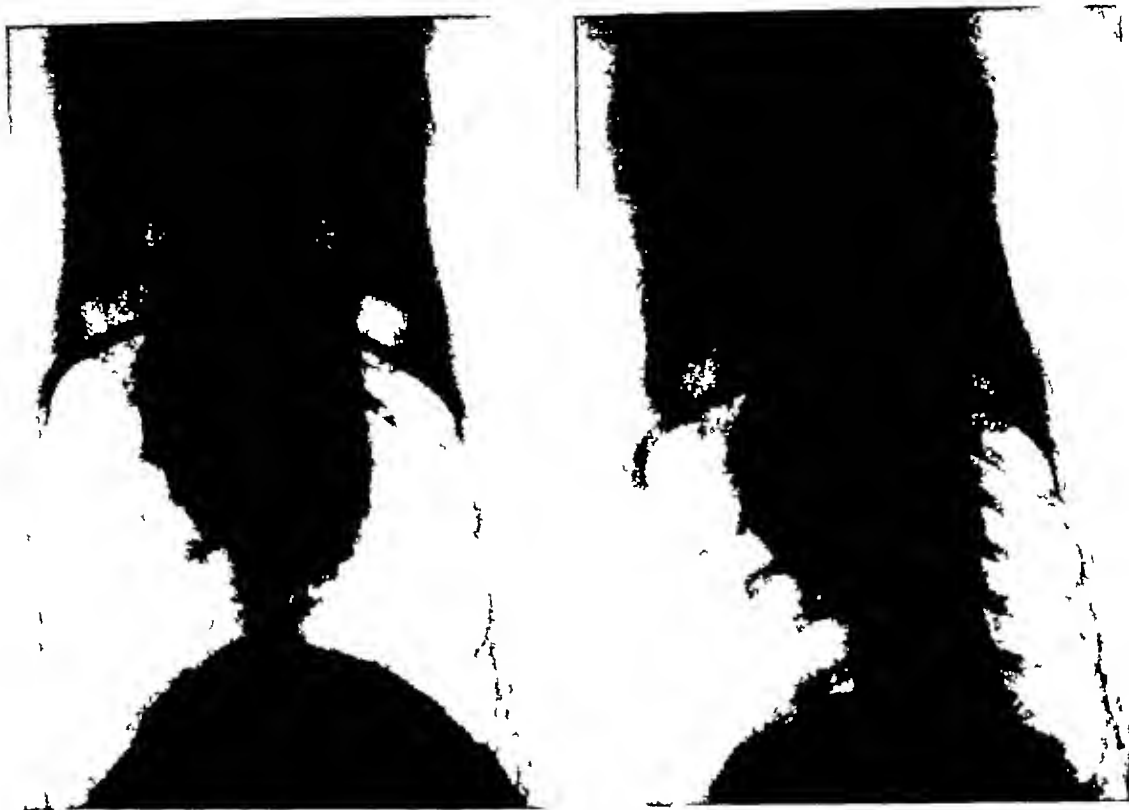


Fig 2 a, left, Normal lung field, b, 20 minutes after injection of 6 cubic centimeters of oleic acid

Provided that the temperature remained constant and that the specimen did not stand too long, the difference *in vitro* did show an appreciable change provided that larger quantities of olive oil were used

The fact that the surface tension determinations varied with variations of temperature and standing of the specimen only occurred to the author after a number of confusing determinations on the same specimen during the same day. This aspect of the problem was easily gone into and was readily solved. The findings were as follows

#### VARIABLES PRODUCED BY STANDING

specimen	Surface tension	After 20 minutes standing
No 10	78.25 dynes	80.5 dynes
No 11	78.35 dynes	81.5 dynes

The variation produced by standing alone would be enough to counteract any possible

accuracy of the method. A far more interesting variation was observed with temperature changes. Variations of about 35 degrees of temperature produced around 8 dynes variation in the surface tension. The results were as follows

#### TEMPERATURE CHANGES USING SAME SERUM

	Degrees C	Dynes
Serum No 3 (without oil)	21.8	88.75
	38.0	86.0
	49.0	83.5
	55.0	81
Serum No 4	21.8	88
	36.5	84
	46.0	83
	57.0	80

These short experiments showed that the numerous variables are too great to be of any real diagnostic value even if the *in vivo* experiments were as promising as the *in vitro* ones





Fig. 3. a, left, Prior to experimentation. b, 5 hours after injection of 5 cubic centimeters of sterile oleic acid.



Fig. 4. a, left, Normal lung field. b, 45 hours after injection of 5 cubic centimeters of sterile oil.

FAT TOLERANCE IN DOGS—  
EXPERIMENTS IN IMMUNIZATION

That animals can be made tolerant to lethal doses of intravenous fat was first shown by Paul and Windholz in 1925. This was later confirmed by Domanig in 1932.

Paul and Windholz used repeated small doses of fat in daily injections. At each injection larger quantities were given. They at first thought that this increased tolerance was due to a greater production of serum lipase. However, careful investigation with the Traube stalagmometer failed to show any such rise. They then concluded that this increased tolerance was due to the acceleration of absorption of the fat by the tissues.

Domanig gave hourly injections of intravenous fat and was also able to create an apparent relative immunity to increasing doses of intravascular fat. He was unable to show any transferable fat dissolving or lipolytic substance created in these animals. He likewise concluded that the increasing doses created an accustomizing reaction of the body to the fat. By careful stool and urine examinations, he showed conclusively that there was no increased elimination which might explain the increased fat tolerance.

The above experimenters used small divided doses given at frequent intervals. The thought occurred to me to give massive sublethal doses with a longer interval between doses in the hope that by using this procedure perhaps the mechanism of fat tolerance might be different.

Paul and Windholz, and Domanig used both olive oil and human bone marrow fat. It appeared to me that if we expect any definite serological reaction, the bone marrow fat from dogs alone should be used in dogs. For this reason bone marrow fat obtained by extracting cut dog bones was used.

It was found that the minimal lethal dose was from 2.2 to 2.5 cubic centimeters per kilogram body weight of the animal.

By weekly injections of increasing doses 4 animals reached a figure of 5 cubic centimeters or more per kilogram body weight before the quantity of fat produced death. One animal received 5 cubic centimeters per kilogram, one 5.5 cubic centimeters, and 2 animals received 6 cubic centimeters per kilogram.

Three dogs were transfused with 65 to 85 cubic centimeters of citrated blood from the animals which had survived 5.5 cubic centimeters of bone marrow fat per kilogram of body weight.

In each instance after the termination of the transfusion, 3 cubic centimeters of dog bone marrow fat were injected per kilogram body weight (a lethal quantity). None of these animals survived. At least for the time being no transferable substance has been found which could be used to transmit a partial immunity or increased fat tolerance from one animal to another. Perhaps none exists and on the other hand perhaps other methods of approaching the problem may isolate it.

CONCLUSIONS

1 The literature shows conclusively that the postmortem table, unfortunately, is not the last court of appeal for fat embolism following fractures.

2 Quantitative blood fat determinations are of no value in the diagnosis, because the physiological variations are too great.

3 Qualitative dark field examinations of the blood should be of great aid in the diagnosis, in the hands of trained microscopists.

4 In the urine examination of suspected cases, only the last few cubic centimeters of a catheterized specimen are valuable.

5 Our uniformity of experimental results makes the author feel that intravenous fat droplets, if present in sufficient quantity, will always produce changes in the lung fields, detectable by the x-ray.

6 The sizzle test, using a platinum loop and a Bunsen burner, is accurate in 1:1400 to 1:1600 dilution. It is very simple and requires no special apparatus nor any complicated equipment.

7 The technique of Sudan III staining of the urine and blood specimens, in order to be accurate, must be done according to the following rules: (a) The stain must be fresh, (b) a high concentration of the dye is necessary to stain the fat droplets, (c) the stain must be permitted to act on the fat for at least 5 minutes in order to stain it well, (d) orange droplets less than 3 to 4 microns are either contamination or undissolved stain,

(e) a drop of stain must be added directly to the slide and not to a test tube specimen.

8. Cardinal and decolin sodium are of no value either as diagnostic or therapeutic drugs.

9. Fat droplets are excreted exclusively through the tubules of the kidney. If the concentration of the fat reaches 0.75 cubic centimeters or more per kilogram body weight.

10. Surface tension studies of the blood serum are of no value in this disease because the variables are too numerous to be satisfactorily controlled.

11. Since all the bone marrow fat extracted from a femur is not sufficient to cause death, the author believes from experimental evidence that oleic acid which is one of the split products of the neutral olein of bone marrow is the probable etiological factor. This substance is seven times as lethal as neutral bone marrow fat, and sufficient quantity could easily be available.

12. Experimentally animals can be made resistant to lethal doses of intravascular fat provided the injections are given in gradually increasing doses. The mechanism of this phenomenon is not clear. Whether it is due to an increased tissue resistance or the formation of an emulsifying agent will require further work.

#### BIBLIOGRAPHY

1. KELLY, R. *Ztschr f orthop Chir* 907 9 60-4
2. BATTY, C. F. *J Am M Ass* 926, 86 446-549
3. BASSO, I. *Ztschr f Biochem* 9 8, 9 22
4. BOWELL, W. W. *J Am M Ass* 6, 67 926
5. BLOOM, W. R. *J Biol Chem* 922, 77 33-73
6. BLOOM, W. R., PELLAN, K. F. and ALLEN, D. M. *J Biol Chem* 927 5 9 205
7. B. KREYER, L. *Vierteljahr f gerichtl Med (supple ment)* 9 2, 30 40-47
8. CALDWELL, G. T. and H. ER, H. L. *Surg Gynec & Obst* 9 7 5 690
9. CARRARA, M. *Friedrich Bi f gerichtl Med* 893, 40 24 270
10. C. TAYLOR, J. *Presse Méd.* 920, 28 6 8.
11. C. BERNI, W. R. *Personal communication*
12. CHER, V. *Berl Klin Wchnschr* 875 593-605
13. DONOVAN, F. *Deutsche Ztschr f Chir* 932, 30 693-703
14. FORTMANN, J. *Monthly Micro. J* 877 8 75-83
15. ELLIOTT, A. W. and MARTIN, C. F. *Ann Surg* 5, 8 390-391
16. F. F. F. *Deutsche Ztschr f Chir* 10 07 450-476
17. GALE, H. *Cornell Veterinarian*, 920, 07 54 5
18. GAGE, S. H. and FEAR, F. A. *Am J Anat* 24 34 5
19. C. H. H. *Arch f L. Med* 6 8 70
20. KERN, Arch. Surg. 924, 9 593-605
21. GROSSMANN, D. *Deutsche Ztschr f Chir* 9 50-24
22. GOSWELL, H. *Yale J Biol & Med* 935 936, 8 50-0
23. JIR, C. F. and SCHROEDER, C. S. *Arch Surg* 934, 33 708-7 1
24. KIMMO, A. M. and SETO, K. *Ztschr f Biochem* 908, 8
25. L. MOORE, F. *Deutsche med Wchnschr* 926, 3 283-285
26. LE CORN, E. R., and G. R. H. T. *Chicago Path Soc* 9 5, 0 5
27. LARSEN, E. P. and MCINTYRE, K. F. *Arch. Surg* 928, 7 70-80
28. LARSEN, E. P. and MOORE, R. M. *Arch Surg* 927 4 6 -661
29. LEXNER, E. *Lehrbuch der allgemeinen Chir* 3 Aufl, 908.
30. LEXNER, E. *Quoted from Flournoy*
31. M. LEXNER, P. *Leçons sur les phénomènes physi de la le. 2, 894.*
32. MILLER, R. E. L. *Wisconsin M J* 930 20 30
33. NICHOL, A. *Zentralbl f Physiol* 907, 03
34. NICHOL, J. L. *Schweiz med Wchnschr* 934, 9 845
35. PATE, M. and WUNDERLICH, F. *Mitt d Grenzgeb d Med Chir* 925, 28 624-65
36. RAVENHILL, E. *Deutsche Ztschr f Chir* 932, 290 4
37. RUTHER, M. *Schweiz med Wchnschr* 907 24 2004-2005
38. RUTHER, B. *Deutsche Ztschr f Chir* 877 8 57
39. RUTHER, E. W. *J Am M Ass* 9 6, 67 637
40. SCHULZ, L. *Zentralbl f Chir* 9 6, 37 42-43
41. SCHULZ, J. *Deutsche Ztschr f Chir* 850, 8
42. SCHROEDER, C. S. *Internal Surg Digest*, 934, 3 95-9 5
43. IDEM. *Arch Path* 930, 28 668-673
44. SIMONDS, J. P. *J Am M Ass* 9 7 69 883
45. SPEED, K. *Fractures and Dislocations* 1st ed. Lippincott, 9 6
46. STODOLSKA, J. L. and DUNN, P. E. *J Biol Chem*, 920, 84 74 748
47. TAYLOR, J. *de chir* 9 4, 267-266
48. V. M. B. *M Arch Surg* 93 3 430-405
49. WARTON, A. S. *Internal Clin* 9 3, 4 71 77
50. WEGGEL, C. *Schweiz med. Wchnschr* 9 3, 4 33 38
51. WELLS, H. G. *Quoted from Ryerson*
52. WELLS, M. *Schweiz med* 9 2, 50 13-30
53. WRIGHT, R. R. *Ann Surg* 932, 96 75-84
54. ZENKER, P. A. *Beitr norm path Anat. d Lander* 80

# EXPERIENCES WITH INTRAMEDULLARY TRACTOTOMY

## IV Surgery of the Brain Stem and Its Operative Complications

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**S**URGICAL procedures upon the various extramedullary segments of the trigeminal nerve for the relief of major trigeminal neuralgia or for intractable facial pain due to other reasons have suffered from several drawbacks. All of these have not been eliminated by either the Frazier-Spiller retrogasserian neurectomy or by the Dandy-Olivecrona method of sectioning the trigeminal root in the posterior fossa. In both of these operations the resulting corneal insensitivity permits the occurrence of neuroparalytic keratitis. The face feels numb and stiff and roughly 5 per cent of patients develop distressing dysesthesias which often cause more suffering than did the original neuralgia.

To avoid these complications, Sjoqvist (6) in 1938 proposed cutting the descending tract of the trigeminal nerve within the medulla oblongata. The rationale for this new method was based on the peculiar anatomy of the intramedullary pathways of the trigeminal nerve. A brief and simple description of the central trigeminal fibers will provide the theoretical background of the operation.

The sensory root of the trigeminal nerve enters the brain stem at the junction of the pons and medulla. Immediately upon the entry the fibers undergo an anatomical separation and a physiological dissociation. The fibers mediating touch sensation turn rostrally and enter the main sensory nucleus of the trigeminal nerve and thence by the secondary neuron ascend to the sensory nucleus of the thalamus. The fibers mediating pain sensation, on the other hand, turn caudally and in company with the spinal nucleus of the trigeminal nerve run throughout the length of the medulla and into the upper cervical spinal cord. In the closed portion of the medulla they lie on the superficial lateral aspect where

they form a distinct elevation, the tuberculum cinereum. The tuberculum cinereum is, in this situation, above the olivary eminence and below the restiform body. An incision into the tuberculum cinereum, therefore, cuts the descending tract of the trigeminal nerve and presumably avoids the important nuclei, tracts, and respiratory mechanisms in this neighborhood.

Since only the pain fibers are interrupted, certain advantages are apparent. Touch sensation is spared, and the face does not feel cold and numb. Neuroparalytic keratitis should not result since some sensation is retained in the eye. The motor component is also spared which makes the operation suitable for bilateral trigeminal neuralgia. Furthermore, Sjoqvist believed that facial dysesthesias would not follow this procedure.

Thirty-five operations of this type have been reported, of which 19 cases have been done in this clinic. Nine patients were originally operated upon by Sjoqvist (7), 3 cases have been reported by Rowbottom, 1 by Jackson and Ironside, 2 by Walker, and 1 by Smyth. The results in 19 cases in terms of relief of facial pain have been reported by Grant and Weinberger (3) as well as an analysis of the sensory phenomena (10), and neurologic sequelae (11).

### SURGICAL TECHNIQUE AND PLACEMENT OF THE MEDULLARY INCISION

Before Sjoqvist performed this operation for the first time, it was thought extremely hazardous to incise the brain stem. As a matter of fact, it was believed that death could ensue if the medulla was accidentally penetrated during the performance of a cisternal puncture. From experiences with intramedullary tractotomy, it is now known that relatively large incisions may be made in the medulla with small risk to life, if carefully placed.

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**Anesthesia**—The premedication used consists of 3 grains of nembutal given at midnight. The morning of operation morphine sulphate grains 1/6 and scopolamine grains 1/150, are given 2 1/2 hours before operation and again 1 1/2 hour before operation. In most instances avertin, 60 to 70 milligrams per kilogram has been used as anesthetic, although in a few cases the premedication was so successful that it was possible to perform the operation with local infiltration of novocain into the scalp. There is an objection to local anesthesia because cutting the tract is painful and the patients move during the section. This can be dangerous since the movement may deflect the operator's hand while the knife blade is in the medulla.

**Operative exposure**—A conventional suboccipital hemilaminectomy is performed. It is not necessary to expose the lateral sinus. It adds to the ease of the subsequent manipulations to rongeur the bone a little past the midline. The entire posterior rim of the foramen magnum must be removed. This is especially important on the side of the projected incision since an adequate lateral view of the medulla is the *sine qua non* of the exposure. In taking away the most lateral bit of the foraminal rim, care must be taken not to injure the vertebral artery which enters the cranial cavity about a centimeter below. Although Sjöqvist, in his operative description, did not mention removing the arch of the atlas we have found that a wider and better view of the medulla is secured by so doing. The dura is opened by radial incisions, and the flaps are tacked to the adjacent muscle. A linear incision is then extended downward to open the dura over the upper cervical cord. The arachnoid membrane of the cisterna magna is torn and the cerebrospinal fluid is allowed to escape. The medulla, with the emerging lower cranial nerve roots, comes into view. In most cases a large looping artery, the posterior inferior cerebellar is seen lying against the side of the medulla just under the cerebellar tonsil. The cerebellar tonsil is gently retracted upward and rostrally by a small spatula protected with moist cotton. There are often small arachnoidal adhesions between the tonsil and the medulla, which may be gently separated without trouble. Oc-

asionally these contain small veins which may be coagulated and cut. The tonsil is retracted until the obex of the fourth ventricle is visualized on the dorsal aspect of the medulla and the emerging rootlets of the ninth and tenth cranial nerves are seen on the lateral aspect (Fig. 1).

**Placement of the incision and the anatomical problems involved**—According to Sjöqvist an anatomical landmark selected to indicate placement of the incision is the lowermost rootlet of the vagus nerve. At this level the point of the knife is inserted into the medulla just dorsal to the rootlet and carried dorsally for 4 millimeters. The depth of the incision is 3.5 to 4 millimeters. This incision severs the descending tract and spinal nucleus of the vagus nerve. However if one studies a number of specimens of the medulla, one is struck by the variations in the number of vagal rootlets and their points of emergence from the medulla. It is this fact which most likely accounts for the several different and contradictory directions that Sjöqvist gives in his description of the site of the medullary incision. For instance he writes (7 p. 98) "The incision is situated immediately caudal to the lowermost vagal filaments and a few millimeters dorsal to them. At this point the descending tract is no more covered by the restiform body. The level corresponds to a border between middle and inferior 2/3 of the eminentia vermis. This corresponds to a level 8 to 10 mm. cranially to the inferior end of the fourth ventricle."

On measuring out these distances on several specimens of the medulla, it was found that a distance of 8 to 10 millimeters above the obex actually corresponded to a level passing through the rostral tip of the olive or in some cases slightly above it. In a number of medullas the lowermost vagal rootlet was at level of the midportion of the olive but not as far rostrally as 10 millimeters above level of the obex. To add to the confusion the author's drawing which illustrates the site of the incision shows it placed about 2 millimeters above the highest vagal rootlet. Furthermore in case protocol 2 the incision was made 10-12 mm. cranially to the inferior edge of the fourth ventricle. In Case 4 the incision

was made 8 millimeters above the level of the obex while in the 7 other cases it was variously described as being placed at the level of the middle or lower third of the olive or at the level of the lowest vagal rootlet. While Sjoqvist states that the restiform body is avoided by an incision at his recommended level (8 to 10 millimeters above the obex) the cross sectional view of the medulla in which he illustrates the extent of the proposed incision (7) shows the lower half of the restiform body included in the transection (Fig 2a)

It is our belief, from experiences with the operation, that the placing of the incision 8 to 10 millimeters above the level of the obex will result in severe or disabling neurological sequelae in a high percentage of cases. These will come from injury to the restiform body or the main and/or lateral cuneate nuclei which are easily exposed to injury at this level. As in cordotomy, the site and extent of the operation must be measured in terms of millimeters and an error of a millimeter or so at this high level in the medulla may result in disastrous consequences. Although Sjoqvist denies that neurological complications occur, except for an occasional paralysis of the recurrent laryngeal nerve due to handling of the vagal rootlets, his case protocols offer evidence to the contrary. In Case 4 the patient following operation felt



Fig 1 Operative photograph of the medulla oblongata. The tonsil of the cerebellum is retracted to expose the lower portion of the fourth ventricle. The incision, which is marked by a black thread placed in it, is located at a level about 4 millimeters caudal to the obex. Only the dorsal half of the incision is seen, the lower half is concealed by the lateral curve of the medulla. This photograph was taken of Case 2.

numbness in his contralateral extremities and in Case 9 the patient's gait was, "more markedly staggering than on admission." One also gets the impression that neurological compli-



Fig 2 a, left, reproduced from Sjoqvist's monograph (7, Fig 32). The extent of the proposed incision indicated by the shaded area involves almost the lower half of the corpus restiforme, Cr. The cross section represents a level at about the middle of the fourth ventricle. b, is a cross section through the medulla taken 4 to 5 millimeters below

the obex and about 2 millimeters caudal to the olive. The extent of the modified incision is shown by the shaded area. At this level the descending tract of the fifth nerve, Tr V, is most superficial and covered only by a thin band of external arcuate fibers, EAF. The spinal nucleus of the fifth nerve, Nu V, is also fairly superficial.

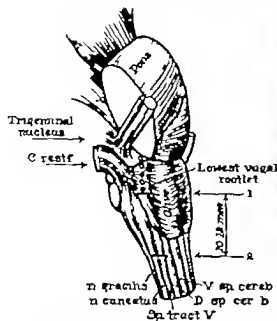


Fig 3 Diagrammatic representation of the fiber tracts in the medulla. Indicates the site of the incision advocated by Sjöqvist. As shown it transects large bundles of fibers running (1) form the restiform body as well as the underlying cuneate nucleus. Indicates the site of the modified incision. (2) this latter place the incision only within a few of the dorsal column fibers and entirely above the restiform body (Adapted from Figure 612, Gray's Anatomy, edited by Lewis, 9 & J. B. Lippincott Co.)

cations may not have occurred in other cases because the incision was not made deep enough to sever the descending tract. This is inferred because in Cases 6 and 7 no sensory alterations resulted in the face and in Cases 1, 2, 3, 5, and 8 complete analgesia was not produced in all three divisions but only in one or possibly two divisions. In 1 of Rowbottom's cases in which Sjöqvist's description was apparently followed the author states that the patient had a "wild ataxia" of the arm following operation. In a case reported by Smith and operated upon by Jackson the patient had postoperative incoordination of the arm and a staggering gait.

Since we have had mishaps of this nature an attempt was made based on a review of the known topographical anatomy of the medulla and the relationship of superficial to deep structures, to modify the site of the incision as to render serious neurological complications unlikely and at the same time to secure an



Fig 4 Prepared specimen of the medulla oblongata. The stippled band outlines the medullary portion of the tuberculum cinereum which contains the descending tract and spinal nucleus of the trigeminal nerve. The (O) encircles the obex of the fourth ventricle which is the primary landmark for locating the medullary incision. Four to five millimeters caudal to it the incision is placed into the tuberculum cinereum as indicated by horizontal. The incision recommended by Sjöqvist is indicated by vertical. The latter still almost invariably involves the restiform body.

adequate facial analgesia. The following anatomical data are presented to explain the rationale of the modification.

The trigeminal nerve enters the lower portion of the pons and penetrates 4 or 5 millimeters until it reaches the lateral portion of the tegmentum. At this point 4 to 5 millimeters beneath the surface of the brain stem and under cover of the middle peduncle it breaks up into the ascending fibers and into the descending fibers which form the descending tract. As the descending tract courses caudally it becomes more superficial and at the level of the middle of the fourth ventricle it is covered only by the restiform body on the dorsal and dorsolateral aspects. It is at this level that Sjöqvist recommends that the tract be sectioned. As the tract descends still more caudally it emerges from under the restiform body and at the level of the obex it is almost on the surface of the medulla and forms a well defined eminence, the tuberculum cinereum. Four to five millimeters below the level of the obex the restiform body is no longer present and the tract is covered laterally by only the external arcuate fibers and the dorsospino-cerebellar fibers. These run in a vertical ventrodorsal or in a vertically oblique direction so that the incision parallels their course (Fig 3).

An incision into the medulla at this level cannot injure the restiform body or the cuneate nuclei and can only injure a few external arcuate and dorsal spinocerebellar fibers (Fig 4). A transection at this level 3 to 4 millimeters deep will encompass all the fibers of the trigeminal tract and will assure an adequate facial analgesia (Fig 2b).

It has been thought that only the fibers from the ophthalmic division descend to the cervical cord and that the fibers from the maxillary division end about the level of the lowest glossopharyngeal rootlets. The mandibular fibers were thought to terminate still higher in the medullary portion of the spinal nucleus (8). In 1 case in which we made the incision into the medulla about 8 millimeters below the level of the obex, a total and lasting analgesia was obtained in all three divisions of the face. This experience serves to prove that all divisions of the face are represented in the tract as low as the level of the upper pyramidal decussation. We feel, therefore, that it is safer to cut the medulla more caudally for the descending tract is most superficial and there are no vulnerable structures to be injured by an incision 3 to 4 millimeters deep.

When we first started to perform these operations 2 years ago, we used the level recommended by Sjoqvist (8 to 10 millimeters above the obex). Severe neurological symptoms followed operation which were first partly ignored since it was thought that they were only transitory. As the cases were followed over a period of many months it became evident that in a number of instances the disturbances persisted and produced considerable disability. It was this experience combined with the opportunity to study several postmortem specimens that caused us to modify the procedure. In order to illustrate the possibilities of injury to the restiform body and cuneate nuclei when making the high incision recommended by Sjoqvist, the following case is cited.

**CASE 1** R. J. Surgical 43547. The patient was a 46 year old male with carcinoma of the tongue and severe intractable pain in the left mandible. In order to relieve his pain it was thought necessary to render his face analgetic as well as to section the ninth nerve and the upper posterior cervical roots. On March 12, 1939, a suboccipital hemicraniectomy was performed, and the arch of the atlas was removed. The upper

three cervical roots on the left side were cut and the glossopharyngeal nerve was sectioned. The tuberculum cinereum was then visualized by retracting the cerebellar tonsil. An incision was made into the tuberculum cinereum at a level 6 millimeters above the obex and approximately dorsal to the lowest vagal rootlet. The incision was 4 millimeters long and 3 to 4 millimeters deep.

**Postoperative course.** The patient was examined the day after operation. There was the anticipated analgesia involving all three divisions of the trigeminal territory. Touch sensation was grossly intact. The analgesia also involved the distribution of the upper three cervical roots. His pain had disappeared. However, there was a marked weakness of the homolateral arm and the patient complained of numbness and tingling in the fingers of the homolateral hand, i.e., homolateral to the side of the incision. There was a mild inco-ordination of the arm. The fingers were so clumsy that he could not hold or handle objects. Postural sensation was seriously impaired in the fingers of the left hand, less so at the wrist and slightly at the elbow. There were pseudoathetoid movements of the extended fingers. There was a mild inco-ordination of the left leg. Eight days later the inco-ordination of the arm was still marked though less than after operation. Postural sensation was still impaired in the hand and it still felt numb and tingling. He was unable to stand unsupported because of ataxia and staggering. He fell to the left. The difficulties in gait and equilibrium were disproportionate to the static cerebellar disturbances in the left leg. When discharged at the end of 2 weeks he was still too ataxic to walk unsupported and there was still inco-ordination in the arm and leg. Two months later and just before his death his wife wrote us that he could not walk because of staggering, that his left hand was still clumsy and that it felt numb.

Perhaps had he lived longer many of his neurological disabilities would have improved because our experience shows that this does occur. The operation, however, disabled him for 2 months. In this particular patient the neurological sequelae were a cheap price to pay for the relief of pain but this case emphasizes the serious complications that may occur with high placed incisions. Undoubtedly the restiform body and cuneate nuclei were injured. Although the neurological sequelae tend to disappear in time, 2 to 4 months' disability is a more serious consideration when dealing with cases of trigeminal neuralgia. Most of the patients operated upon in whom the Sjoqvist incision was used had considerable postoperative neurological disturbances. We have now performed 4 operations in which the incision was placed in the tuberculum cinereum 4 to 5 milli-



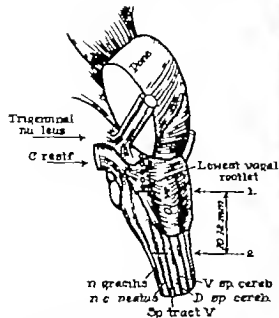


Fig. 3. Diagrammatic representation of the fiber tracts in the medulla. 1 indicates the site of the incision advocated by Spöqvist. 2 shows it transecting large bundles of fibers running 1 form the restiform body as well as the underlying cuneate nucleus. 2 indicates the site of the modulated incision. 1 this latter place the incision only necks few of the dorsal column fibers and entirely spares the restiform body. (Adapted from Figure 613, Gray's Anatomy, edited by Lewis, 9 & J. B. Lippincott Co.)

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Fig. 4. Prepared specimen of the medulla oblongata. The stippled band outlines the medullary portion of the tuberculum cinereum which contains the descending tract and spinal nucleus of the trigeminal nerve. The O indicates the obex of the fourth ventricle which is the primary landmark for locating the medullary incision four to 5 millimeters caudad to it the incision is placed into the tuberculum cinereum as indicated by numeral 1. The incision recommended by Spöqvist is indicated by numeral 2. The latter sits almost invariably in oblique the restiform body.

adequate facial analgesia. The following anatomical data are presented to explain the rationale of the modification.

The trigeminal nerve enters the lower portion of the pons and penetrates 4 or 5 millimeters until it reaches the lateral portion of the tegmentum. At this point 4 to 5 millimeters beneath the surface of the brain stem and under cover of the middle peduncle it breaks up into the ascending fibers and into the descending fibers which form the descending tract. As the descending tract courses caudally it becomes more superficial and at the level of the middle of the fourth ventricle it is covered only by the restiform body on the dorsal and dorsolateral aspects. It is at this level that Spöqvist recommends that the tract be sectioned. As the tract descends still more caudally it emerges from under the restiform body and at the level of the obex it is almost on the surface of the medulla and forms a well defined eminence, the tuberculum cinereum. Four to five millimeters below the level of the obex the restiform body is no longer present, and the tract is covered laterally by only the external arcuate fibers and the dorsospino-cerebellar fibers. These run in a vertical ventrodorsal or in a vertically oblique direction so that the incision parallels their course (Fig. 3).

straight blade to make the incision, we early found that it was difficult, if not impossible, to see the point of the blade enter the medulla. Using a curved blade No. 12 with a sharp point, one has a full view of the knife point and therefore better control over the length and depth of the incision. A bit of wax may be placed on the knife 4 millimeters above the point, to serve as a guard.

#### NONNEUROLOGICAL COMPLICATIONS

For 1 to 3 days after operation most patients have a marked headache due to blood in the posterior fossa, loss of cerebrospinal fluid, and air in the subarachnoid space. Five patients developed hiccoughs on the second to fifth day. These lasted 3 to 9 days and were refractory to all treatment although carbon dioxide inhalations gave temporary relief. In 2 instances they were very exhausting. No difficulties in swallowing or speech were encountered. In Sjöqvist's series there were 3 instances of recurrent laryngeal paralysis. We have not seen this complication. Although the medulla is necessarily incised in this operation we have not seen any respiratory difficulties on the operating table or thereafter.

#### MORBIDITY AND MORTALITY

The periods of postoperative hospitalization ranged from 8 to 21 days and averaged 14 days. Two patients with oral carcinoma died from late postoperative pneumonia on the thirteenth and seventeenth postoperative days. At necropsy, one patient showed a widespread pulmonary carcinomatosis and the other multiple pulmonary abscesses. One patient operated upon for a painful carcinoma of the cheek developed a postoperative psychosis which persisted and necessitated his removal to an institution.

#### SUMMARY AND CONCLUSIONS

The results of the operation in terms of relief of pain have been dealt with in other publications but are briefly summarized in Tables I and II.

Intramedullary tractotomy is neither a difficult nor a complicated operation but requires an intimate knowledge of the topographical and internal anatomy of the medulla oblong-

ata. At present, the procedure is just moving out of the experimental stage. Similar hazards and complications were encountered in the early development of anterior cordotomy and it is expected that apprentice fees must be paid in order to develop, modify, and perfect the technique.

Although we do not, at present, feel that the operation is acceptable as a routine procedure in cases of trigeminal neuralgia, various conditions exist in which it might be considered the operation of choice. In cases of severe trigeminal neuralgia affecting the upper or upper two divisions or all three divisions of the face, tractotomy avoids the possibility of neuroparalytic keratitis which might result from the complete section of the root required to relieve the pain. In cases in which neuralgia has developed on the second side after a previous retrogasserian neurectomy has been performed, tractotomy avoids involvement of the motor component and preserves masseter function. In neurotic persons in whom one might expect severe distress from postoperative numbness if the sensory root were sectioned, tractotomy is indicated since there are fewer unpleasant subjective sensations in the face. Not infrequently careful questioning shows that a patient has a burning pain in the face between the paroxysms of true neuralgia. Our experience with such cases has taught us that this burning pain may persist in the anesthetic area and even be accentuated by the presence of the anesthesia. Medullary tractotomy relieves the paroxysmal pain without producing subjective sensory changes in the face. If the complete anesthesia produced by sensory root section could thus be avoided the burning paresthesia might be much less annoying. It has its widest application in cases of malignant disease about the head where pain makes it desirable to render the face analgetic. Since it is often necessary also to section the ninth nerve and posterior cervical roots, tractotomy can be easily done through the same exposure.

Most of the advantages claimed for the operation have been confirmed in our experience. Touch sensation for all practical purposes is preserved, and the patients are hardly aware that their faces have been made analgetic. No cases of neuroparalytic keratitis have been ob-

TABLE I.—SUMMARY OF DATA ON THE IMMEDIATE POSTOPERATIVE STATUS OF 19 CASES OF TRACTOTOMY

	Trigeminal sensory division	Malgouyres division
Complete relief of pain	7	9
Partial relief of pain		
No relief of pain		
Satisfactory facial analgesia	7	9
Unsatisfactory facial analgesia		3
Marked neurological disturbances	4	3
Moderate neurological disturbances		3
Minor neurological disturbances		
No neurological disturbances		

1, not known.

meters below the level of the obex. In comparison with the case described we cite one such patient operated upon with the modification in the placement of the incision.

CASE 1. E. Surgical 3605. The patient was a 5-year-old woman who had suffered with major trigeminal neuralgia, second and third divisions, for 3 years. She had received temporary relief from alcoholic injections but finally demanded permanent relief. An intramedullary tractotomy was performed April 24, 1940. The obex was used as the landmark and the tuberculum cinereum as transected at level 4 to 5 millimeters below the obex and about millimeters below the olive (Fig. 1).

Postoperative course. Six hours after operation the patient was clear and co-operative. Examination disclosed a slight inco-ordination of the homolateral arm. Her grip was good and there were no subjective sensations in the hand. Postural sensation was intact. By the end of 24 hours the inco-ordination had practically disappeared in the arm. There was complete analgesia in all 3 divisions of the fifth nerve with gross preservation of touch sensation. When put on her feet on the third postoperative day she was unable to walk and fell promptly to the right side. Again the disturbances in equilibrium and gait were disproportionate to the static cerebellar signs for there was only the trace of a heel to knee ataxia when tested in bed. By the fifth postoperative day she was able to walk unsupported, although she frequently staggered to the right side. Her gait rapidly improved and by the twelfth postoperative day there was little evidence of disturbance. The Romberg sign was not present. There was no inco-ordination in either of the right extremities. One month after operation she was performing full household duties. Her only neurological complaint was slight incoordination in descending steps. Two months after examination she was examined and found to be neurologically normal. Her pain was entirely relieved and there was complete analgesia of the three trigeminal divisions.

While mild neurological disturbances were present after operation they were only tran-

TABLE II.—SUMMARY OF AVAILABLE FOLLOW UP DATA ON 15 CASES OF TRACTOTOMY 1 TO 13 MONTHS POSTOPERATIVE

	Trigeminal sensory division	Malgouyres division	Not known
Complete relief of pain	4	5	
Partial relief of pain		3	
No relief of pain			
Satisfactory facial analgesia	4	3	4
Unsatisfactory facial analgesia			
Marked neurological disturbances			
Moderate neurological disturbances			
Minor neurological disturbances	4	4	
No neurological disturbances			
Subjective facial sensations	3	4	5
Objective facial sensations	3	4	

A Craig hospital stay 14 days—Range 8—

\*The last six did not demonstrate absence of C X II

sient and she left the hospital essentially a normal person. These transient symptoms were probably due to cutting of a few spinocerebellar and arcuate fibers and to the regional edema of the medulla. This case typifies the differences in the postoperative course when the incision is made low in the medulla as compared to the previous case in which it was made higher. Neurological compensation apparently is made readily after injuries to the spinocerebellar tracts and arcuate fibers whereas the defects are more profound and less recoverable when the restiform body or cuneate nuclei are injured. This has been shown experimentally in monkeys by Ferraro and Barrera.

Before ending the section on the surgical and anatomical problems brief mention should be made of several other difficulties encountered in the course of medullary surgery. Occasionally thick congenital or small vessels may be clustered over the area selected for the incision. This forces one to make the incision a millimeter or so away. We have adopted the policy of moving the incision caudally the required distance since the descending tract remains superficial throughout the lower medulla. It is unwise to coagulate these vessels on the medulla since the electric current is carried along the vessels into the brain stem and might produce serious results. If the incision is made into an avascular area, hemorrhage never occurs. Although Sjögqvist used a

straight blade to make the incision, we early found that it was difficult, if not impossible, to see the point of the blade enter the medulla. Using a curved blade No. 12 with a sharp point, one has a full view of the knife point and therefore better control over the length and depth of the incision. A bit of wax may be placed on the knife 4 millimeters above the point, to serve as a guard.

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Most of the advantages claimed for the operation have been confirmed in our experience. Touch sensation for all practical purposes is preserved, and the patients are hardly aware that their faces have been made analgetic. No cases of neuroparalytic keratitis have been ob-

served nor have we even witnessed reddening of the conjunctiva. In the majority of cases, even with complete analgesia of the ophthalmic division a blink reflex may be elicited. While pain sensation is lost in the cornea and the affective component of corneal irritation is absent, the patients are able to feel a stimulus on the cornea, the sensation being described as a light touch or tickle. Although it is too early to speak with assurance about postoperative dysesthesias we have 4 patients with subjective facial sensations. In no case have they spontaneously complained of these sensations and in no instance have they been of the disagreeable or distressing character as are often a source of distress after sensory root section. One patient had slight burning sensations about the eye which were annoying but perfectly tolerable. One had prickling and tingling sensations for which he rubbed his face with liniment. One woman complained of brief paroxysms of burning at the angle of the mouth, and one stated that he had chilly sensations and the illusion that his nose was watering.

Theoretically there is no reason why interruption of the intramedullary trigeminal pathways should not be followed by dysesthesias. It is well to recall in this connection the fact that thromboses of the posterior inferior cerebellar artery which always involve the descending tract of the trigeminal nerve, are accompanied, in the majority of cases, by severe burning dysesthesias (12). Only a larger

experience will determine whether they occur following surgical transection of the tract.

#### BIBLIOGRAPHY

1. FERRARO, A. and BARKER, S. E. The effects of lesions of the dorso-spinocerebellar tract and corpus reticulare in the macaca rhesus monkey. *Brain*, 93S: 58-74.
2. Idem. Effect of lesions of the juxtarestiform body (I A K. bundle) in macaca rhesus monkeys. *Arch. Neurol. & Psychiat.* 93S, 35-41.
3. GRANT, F. C., and WERNICKE, L. M. Experiences with intramedullary tractotomy. I. Summary of the operative results and complications. To be published.
4. JACKSON, H. and IRONPETER, R. Left trigeminal pain treated by means of Sjöqvist's medullary trigeminal tractotomy. *Proc. Roy. Soc. Med.* 93S, 3 pt. 9.
5. ROXBOROUGH, G. F. Treatment of pain in the face by intramedullary tractotomy. *Brit. M. J.* 93S, 1073.
6. SJOQVIST OLAV. Eine neue Operations Methode bei Trigeminal Neuralgie. Durchschneidung des Tractus Spinalis Trigeminal. *Zentralbl. Neurochir.* 93S, 274.
7. Idem. Studies on pain conduction in the trigeminal nerve. A contribution to the surgical treatment of facial pain. *Suppl. 7 Acta psychiat. et neurol.* 93S.
8. SMITH, G. E. The systemization and central connections of the spinal tract and nucleus of the trigeminal nerve. *Brain* 93S, 6-4.
9. WALLACE, E. A. Anatomy, physiology and surgical considerations of the spinal tract of the trigeminal nerve. *J. Neurology* 93S, 34.
10. WERNICKE, L. M. and GRANT, F. C. Experiences with intramedullary tractotomy. II. Studies in resection. In preparation for publication.
11. Idem. Experiences with intramedullary tractotomy. III. The immediate and late neurologic disturbances. In preparation for publication.
12. WERNICKE, L. M. Tractotomy (Sjogqvist) viewed in the light of the pathology of the medulla oblongata. *Acta psychiat. et neurol.* 93S, 4-243.

# EXPERIMENTAL CEREBRAL TRAUMA

## II — Further Observations on the Fluid Content of the Brain Following Trauma to the Head

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IN experiments previously reported (2), it was found that there was little, if any, significant alteration of the fluid content of various parts of the dog's brain after trauma to the head sufficiently severe to produce a marked rise in cerebrospinal fluid pressure. Since, theoretically, with skull and dura mater intact, an increase in tissue fluid volume could occur only at the expense of a diminution in intracranial blood or cerebrospinal fluid volume, similar experiments have been made with one hemisphere of the brain freely exposed. These experiments offer the additional advantage of comparison of the exposed with the unexposed hemisphere, as well as with normal control values.

### METHODS

Anesthesia, position of the head, and methods of sacrifice of the animals and isolation of specimens of cerebral gray and white matter, cerebellar gray matter and brain stem are exactly as described in the previous study (2). Specimens of cerebral gray and white matter were removed from both hemispheres in all experiments. Fluid content was determined by drying to constant weight at 60 degrees C as before. Trauma was administered by dropping a 1000 gram weight from a distance of 60 inches twice in rapid succession. This degree of trauma has been found to produce consistently a marked elevation in cerebrospinal fluid pressure when skull and dura are intact. Cerebrospinal fluid pressure and femoral arterial pressure were determined as in the preceding study.

Two types of experiments were performed. In the first type, the entire left cerebral hemisphere was exposed, the dura being incised in stellate fashion and its flaps laid back. The

exposed brain was lightly covered with a flat sheet of warm, moist cotton which was moistened from time to time with warm physiological saline solution. No trauma was administered. After intervals of from 4 hours to 5½ hours, specimens were rapidly removed for determination of fluid content. Seven such experiments were performed.

In the second type of experiment, trauma was administered as described and the left hemisphere was exposed immediately afterward. The animals were sacrificed and specimens were secured 4 hours after trauma in 2 experiments, 4½ hours after trauma in 2 experiments, and 8 hours after trauma in 2 experiments. No visible hemorrhage was present in any experiment.

### RESULTS

*Left hemisphere exposed. No trauma.* The arterial blood pressure was not significantly altered during any experiment. The cerebrospinal fluid pressure was very slightly elevated in one animal (Dog T 67) and elevated 185 millimeters of water above the control level in another (Dog T 68). In the latter the cotton pad over the left hemisphere was adherent to the brain at the end of the experiment. When it was gently removed, a gush of fluid followed and the cerebrospinal fluid pressure fell to the control level. In the remaining experiments, the cerebrospinal fluid pressure was not altered. Bulging of the exposed hemisphere at the end of the experiments was absent in 5 dogs, slight in 1 dog, and marked in 1 dog.

The fluid content of the brain specimens is given in Table I. Although there were occasional individual variations, the findings, for the most part, were surprisingly uniform as was found in the previous study. No significant difference could be demonstrated between the fluid contents of corresponding specimens

TABLE I.—LEFT HEMISPHERE EXPOSED—NO TRAUMA

Dog number	Left cerebral gray matter—percentage of fluids	Left cerebral white matter—percentage of fluids	Right cerebral gray matter—percentage of fluids	Right cerebral white matter—percentage of fluids	Cerebellar gray matter—percentage of fluids	Brain stem—percentage of fluids	Time hrs
T 6	76.6	69	75	70	70	70	5
T 6	76.6	65	77	73	70	69	
T 41	60		6		80.5		14
T 6	70		6	70	80		
T 67	77	66	76	6	79.5	69	
T 60	70	60	80	66.6	84	77	5
T 69	8	66	6	67	80	70	5
Average	70	66	79.5	69.5	79.9	70.9	

TABLE II.—TRAUMA—LEFT HEMISPHERE EXPOSED

Dog number	Left cerebral gray matter—percentage of fluids	Left cerebral white matter—percentage of fluids	Right cerebral gray matter—percentage of fluids	Right cerebral white matter—percentage of fluids	Cerebellar gray matter—percentage of fluids	Brain stem—percentage of fluids	Time hrs
T 70	78	67.3	70.6	67	70	70.6	5
T 71	6	69	73.3	69.6		7	6
T	78	67	73.6	64.7	70	69	
T	78	66	74.6	66	70.6	68	
T	79	67	70	66	70	70	5
T 75	80	66.6	70.6	66	70.6		
Average	79	67	70	66.6	70.7	70.4	

from the left and right hemispheres. Average findings were almost identical in the two hemispheres and they also corresponded very closely with the findings in normal control animals, as will be pointed out later.

*Left hemisphere exposed. Severe trauma.* The arterial blood pressure showed a transitory fall followed by a slight elevation immediately following trauma. Otherwise it was not significantly altered. The cerebrospinal fluid pressure was not measurably elevated during any of the experiments, doubtless due to the open wound through which fluid could freely pass. The exposed left hemisphere bulged moderately in 4 experiments and not at all in 1. In the single remaining experiment (Dog T 70) the brain was actually shrunken and retracted from the dura by the end of the experiment. In this animal, the respirations rose from a control rate of 30 to 80 per minute 1 hour after trauma, then slowly fell to and remained at, 40. The dog was moderately cyanotic, but the

arterial blood pressure maintained a constant normal level.

The fluid contents of the specimens from the dogs' brains are shown in Table II. The uniformity of the various values is even more striking than in the untraumatized animals. In every experiment, there were almost identical values for corresponding specimens from the two hemispheres, and the average findings are virtually the same as normal control values (see below).

For purposes of comparison a composite table of averages is presented in Table III. The extremely close correspondence of values for the respective specimens in the different groups of experiments is self-evident.

#### SUMMARY AND CONCLUSION

In an excellent study of traumatized human brains, Shapiro and Jackson have found actually subnormal values for the water content of traumatized brains. Using the iron determination method, they also have shown that the

TABLE III.—COMPOSITE TABLE OF AVERAGES

Type of experiment	Number of experiments	Left cerebral gray matter—percentage of fluids	Left cerebral white matter—percentage of fluids	Right cerebral gray matter—percentage of fluids	Right cerebral white matter—percentage of fluids	Cerebellar gray matter—percentage of fluids	Brain stem—percentage of fluids
Normal controls		70	66			70.6	70
Trauma, no operation		70	66			70	71
Left hemisphere exposed, no trauma		70	66	70	66	70	70
Left hemisphere exposed—trauma		79.2	67	70	66	70.7	70.4

\*Experiments reported in preceding paper (5).

intracerebral blood volume, whether intravascular or extravascular, is greater than normal in such brains (Pilcher, 2) They state, "In the traumatized head the brain is accordingly swollen but not edematous, the swelling is not due to increased water but to increased blood content "

Alexander and Looney studied the brains of a series of patients who died in a psychiatric hospital They concluded that the water content of the brain is not "positively correlated with edema or atrophy of the brain " It is apparent that the contradiction between these two quotations is one of terminology and not of fact The *American Illustrated Medical Dictionary* defines "edema" as "swelling due to an effusion of water liquid into the connective tissue," but Alexander and Looney apparently employ the term to describe brains the size of which is greater than normal They state, "Atrophy or edema of the brain can be meas-

ured quantitatively only by the differential ratio of skull capacity to brain volume or brain weight " The findings of Alexander and Looney do not offer proof of the existence of "cerebral edema," within the meaning of the definition quoted

The experiments reported in this paper clearly demonstrate the marked stability of the fluid content of brain tissue Under these experimental conditions, no significant change in fluid content has been produced

#### REFERENCES

- 1 ALEXANDER, L, and LOONEY, J M Physicochemical properties of brain, especially in senile dementia and cerebral edema Differential ratio of skull capacity to volume, specific weight, water content, water binding capacity and  $p^H$  of the brain Arch Neurol & Psychiat, 1938, 40 877
- 2 PILCHER, C Experimental cerebral trauma The fluid content of the brain after trauma to the head Arch Surg, 1937, 35 512
- 3 SHAPIRO, P, and JACKSON, H Swelling of the brain in cases of head injury Arch Surg, 1939, 38 443



# PLASMA PROTHROMBIN VALUES OF MOTHERS AND INFANTS AT DELIVERY

## Further Studies Including Comparative Values of the Umbilical Arteries and Veins

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THE widespread interest in prothrombin and vitamin K deficiencies has been responsible for several studies on the relationship of these deficiencies to the hemorrhagic diseases of the newborn. The simple clinical method of Quick (1) and Stanley Brown and Bancroft (16, 17) or one of its modifications (11, 12, 13) and the more complicated two-stage titration method of Warner Brinkhous and Smith (19, 23) have been the favorite procedures for the estimation of prothrombin deficiency and therefore indirectly in certain instances of the vitamin K deficiency. At the time of birth, by the Warner method the blood prothrombin has been shown by Brinkhous, Smith, and Warner (4) by Owen Hoffman, Ziffren, and Smith (9) and by Hellman and Shettles (5) to be only about one-quarter that of the normal adult. By the Quick method, however, this deficiency is not so apparent since an increase in the convertibility of prothrombin into thrombin may compensate in part for the deficiency of the former (9). With their method Quick and Grossman (14, 15) found, however, that the prothrombin values of the newborn varied between 60 and 70 per cent of normal.

The available evidence also indicates that in many infants a marked fall in the level of prothrombin may occur 2 or 3 days after birth (9, 14, 15, 20, 21). A gradual rise in the prothrombin level during the next week normally occurs, but this change may be accelerated by the oral administration of vitamin K (18). It is during these first days of life, therefore, when the plasma prothrombin is low that hemorrhage is apt to occur.

Employing the method of Warner Brinkhous and Smith (19, 23) Hellman and Shettles (5) were the first to compare the prothrombin levels of mother and infant. They found that the concentration of prothrombin in normal full term infants averaged less than one-quarter that in the mothers. Norris and Rush, using the Quick method, found that in the case of 50 mothers and their babies the average level of the babies was 63 per cent of the normal controls and that of the mothers 140 per cent when 25 per cent diluted plasmas were compared as against 85 per cent and 117 per cent, respectively, when undiluted plasmas were compared.

Hellman and Shettles (5) likewise noted that the level of plasma prothrombin tended to be even lower in immature infants than in full term babies. Kato and Poncher (7) however found no correlation between the infant's maturity and the prothrombin level of the blood as measured by the micro-prothrombin method of Kato (6). When the prothrombin level by this method was determined on successive days following birth a greater fluctuation of the values was observed in the blood of the premature than in the mature infants.

The cause of the low prothrombin content in the cord blood of the fetus and the apparent fall in the plasma prothrombin level of many infants after birth has not been determined. Norris and Rush suggested that since the prothrombin concentration of mothers at delivery averaged above normal a deficiency of maternal vitamin K probably is not responsible for the low prothrombin of the fetuses. Since the rôle of the liver in elaborating prothrombin from vitamin K has been established

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in experimental animals (2, 14, 15, 19, 22, 23), it has been assumed that the liver of the fetus and newborn is likewise responsible for the formation of prothrombin (14, 15). During intra-uterine life, therefore, vitamin K must be supplied to the fetal liver by way of the mother, but after delivery this source of supply is abruptly removed. Quick (14, 15), therefore, believed that this sudden removal of vitamin K is responsible for the fall of plasma prothrombin during the first days of life. Since Almquist and Stokstad have shown that in the intestinal tract of chicks bacteria may synthesize vitamin K, Quick (14, 15) suggested that when the bacterial flora of the infant's intestinal tract is established vitamin K may be produced by bacterial activity in the intestines. The time when vitamin K thus becomes available corresponds to the time when a rise of the prothrombin level normally occurs.

Because of these uncertainties it was thought important to study a large series of cases in order to determine whether any relationship exists between the prothrombin levels of individual mothers and babies. It also seemed advisable to ascertain whether the prothrombin levels of umbilical arteries and veins are identical in individual cases.

#### METHODS

In the comparison of the individual maternal and infant prothrombin levels, 35 additional cases were added to the original 50 cases of Norris and Rush. All prothrombin values were determined by the method of Quick (16, 17). In the 35 new cases the plasma prothrombin was determined not only in the umbilical vein but also in the umbilical artery. For this purpose blood was collected by the method of Boyd and Wilson. At the time of delivery the umbilical cord was sectioned without clamping 10 to 12 centimeters from the fetus. Blood which ran freely from the placental end of the cord was assumed to be largely from the umbilical vein and blood which spurted from the fetal end was assumed to be from the umbilical artery. Collected simultaneously in separate paraffin-lined beakers, the specimens were immediately mixed in test tubes with the appropriate amounts of sodium oxalate solution. Blood was also col-

lected at once by venipuncture from the mother. In the preparation of the solution of thromboplastin we have followed Quick's modification (11, 12, 13) of his original method in regard to heating the saline mixture and the omission of the oxalate solution from the saline preparation of rabbit brain, but we have continued to use normal hospital workers as controls on each day that determinations were made instead of using Quick's formula for computing the prothrombin values of unknown plasmas. Our experience has been in agreement with Pohle and Stewart's in that the 0.025 molar calcium chloride solution used by Quick often gives slower clotting times than solutions of lower concentration. Consequently, in the last 17 cases we have employed 0.005 molar calcium chloride solution for all determinations. Although the speed of clotting with this concentration is increased the relation between unknown and control appear to be maintained in the same proportion. In all cases we have compared not only the undiluted plasmas of the unknown with the dilution values of the control, but we have also compared the 25 per cent diluted plasmas of each. For interpolation of these dilutions and for the evaluation of an unknown undiluted plasma which clots faster than the control, we have used the formulas of Norris and Rush. In 22 of the last 35 cases the volume of packed erythrocytes in the blood of umbilical artery and vein was also measured.

#### RESULTS AND COMMENTS

The prothrombin values of 35 additional mothers and babies at delivery were averaged with the 50 mothers and 51 babies (including one pair of identical twins) previously reported by Norris and Rush. Prothrombin determinations on blood from only the umbilical veins of the babies were included in the series. In Table I the average prothrombin value of undiluted maternal blood plasma is seen to be 111 per cent and that of the fetal blood to be 77 per cent of normal. The average prothrombin value, when the plasmas diluted to 25 per cent are compared, is seen to be 136 per cent and 64 per cent, respectively. In the first 50 cases reported a tendency for dilution of the plasmas to increase the value

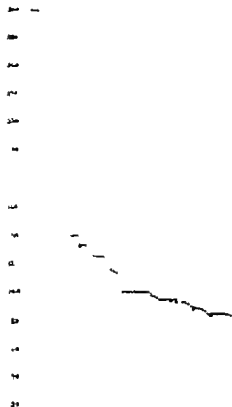


Chart Undiluted plasmas Comparison of individual prothrombin values in percentage of normal in 85 mothers and their babies. Solid dots are maternal, thick curves are fetal values.

of prothrombin in the case of the mothers and to diminish it in the case of the babies as compared to the normal controls was also observed. The explanation for this difference is not apparent, but it has been suggested that dilution of the plasmas may increase the accuracy of the test (8, 9, 14, 15). At any rate the low prothrombin level of infants at birth

does not appear to be caused by vitamin K deficiency in the mothers.

It is of interest that so many of the maternal plasmas appeared to have higher than normal prothrombin values. In the case of the undiluted plasmas 31 were greater than the respective controls and in the 25 per cent diluted plasmas 65 of the 85 maternal plasmas were greater than the controls.

Little has been said in the literature of the possibility that certain individuals may have greater than normal prothrombin values. Poble and Stewart have found that with the Quick test normal plasma will clot in 10 seconds in the presence of an optimal calcium concentration but this time is the minimum unless the plasma is grossly lipemic when slightly faster times may be obtained. Such findings imply at any rate that if clotting is faster than normal the increased speed is not due to more than a normal amount of prothrombin. Even by varying the amount of added calcium in an effort to find the optimal concentration, as suggested by Poble and Stewart we have been unable to obtain for normals minimum clotting time approaching 10 seconds. The clotting time for normal undiluted plasmas, depending upon the solution of thromboplastin used, varies between 12 and 14 seconds in our hands. In a number of cases in which the clotting time of the mother's plasma was faster than that of the normal control varying the calcium concentration did not reduce the clotting time of the normal to that of the mother's plasma. None of these plasmas, furthermore, was lipemic. It appears to us, therefore, that if the increased speed of clotting of many of the maternal plasmas is not due to increased amounts of prothrombin the factors responsible for this phenomenon are as yet undetermined.

TABLE I—A COMPARISON OF THE SPREAD OF THE PROTHROMBIN VALUES FOR MATERNAL AND VENOUS CORD BLOOD OF 85 MOTHERS AND 86 BABIES IN PERCENTAGE OF NORMAL

	100% Plasmas		12% Plasmas	
	I Maternal blood %	II Venous blood %	I Maternal blood %	II Venous blood %
Maximum	500		270	65
Minimum	44	9	0.4	0
Mean		77	36	64

TABLE II—A COMPARISON OF THE SPREAD OF THE PROTHROMBIN VALUES FOR ARTERIAL AND VENOUS CORD BLOOD OF 35 BABIES IN PERCENTAGE OF NORMAL

	100% Plasmas		12% Plasmas	
	I Arterial blood %	II Venous blood %	I Arterial blood %	II Venous blood %
Maximum	60	30	0.3	0.6
Minimum	7	9	7	9
Mean	60	66	54	65

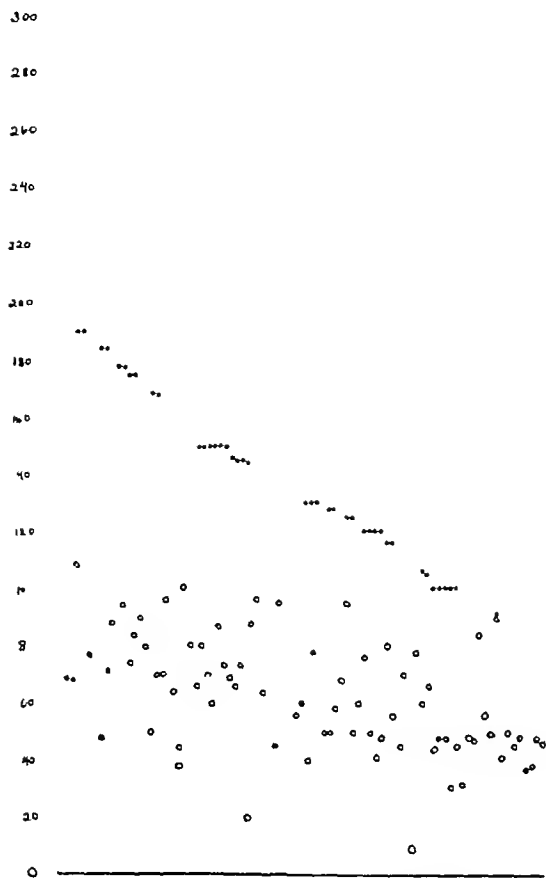


Chart 2 Twenty five per cent diluted plasmas. Comparison of individual prothrombin values in percentage of normal in 85 mothers and their babies. Solid dots are maternal values, circles are fetal values.

In Charts 1 and 2 the individual prothrombin values of mothers and babies at delivery in percentage of normal are compared. Chart 1 is a comparison of the undiluted plasmas and Chart 2 of the 25 per cent dilutions. The solid dots are the maternal prothrombin values, arranged in diminishing order of percentage, and the circles are the prothrombin values of blood from the umbilical veins of the respective infants. From these charts it is quite apparent that there is no correlation between the amount of the plasma prothrombin of individual mothers and babies. In the case of the undiluted plasmas in Chart 1 some of the infants even have higher values than their mothers. In Chart 2 none of the infant prothrombin values exceed their mothers' prob-

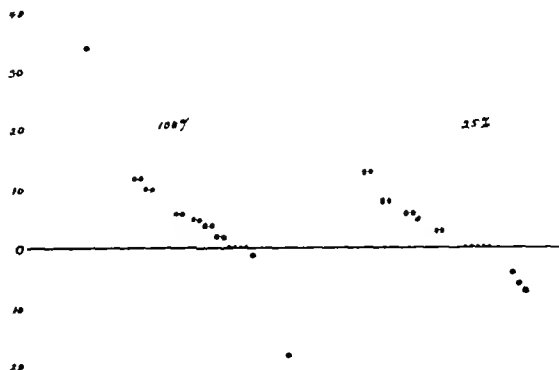


Chart 3 Percentage differences of prothrombin values between individual umbilical arteries and veins in the case of undiluted and 25 per cent diluted plasmas. Above the zero line are those cases in which the value of the vein exceeded the artery, below the line those in which the artery exceeded the vein, and on the line those in which the artery and vein were equal. Thirty five cases.

ably because of the tendency of dilution to increase the spread in the prothrombin levels of mothers and babies. It may be concluded, therefore, that the amount of plasma prothrombin in the infant at delivery is not directly dependent on the amount of maternal prothrombin.

The prothrombin values in blood from the umbilical artery and vein were compared in the 35 additional cases which we are reporting. In Table II it will be seen that the mean prothrombin value of blood from the umbilical veins exceeds that of the umbilical arteries by 6 per cent in the undiluted plasmas and by 11 per cent in the 25 per cent diluted plasmas. In Chart 3 the differences in veins and arteries of the 35 cases are plotted. Above zero are plotted the differences in percentage of those cases in which the plasma prothrombin is greater in the vein than in the artery and below zero those cases in which the value of the artery is greater than in the vein. On the zero line are those cases in which the plasma prothrombin is identical in artery and vein. It will be seen that in 24 of the 35 cases the value for the vein exceeds the artery. Although these cases are too few and the spread of values is too great for statistical analysis, especially when it is possible that the Quick test is not accurately quantitative, the number of cases in which the plasma prothrombin is higher in

the vein than in the artery is great enough to indicate that similar results might be obtained in a large series of cases. If it is assumed therefore for purposes of discussion that these results are not due solely to chance and are a definite indication of differences in the artery and vein, several possible explanations should be considered.

The first possibility is that absorption of fluid from the fetal circulation through the placenta into the maternal circulation might increase the concentration of prothrombin in the plasma of the umbilical vein. In 22 of the 35 cases the volume of packed erythrocytes was measured. In 3 cases the volumes were identical. In 10 cases the volume was greater in the artery than in the vein and in 9 cases the volume was greater in the vein than in the artery. The usual variation was not greater than 1 per cent. Hemocentration therefore is not a significant factor in increasing the concentration of prothrombin in the umbilical veins.

It may be that factors other than prothrombin which influence the speed of clotting are responsible for the apparent differences in the prothrombin values of arteries and veins. Poble and Stewart have shown that changes in the calcium concentration affect the speed of clotting and there is reason to suppose that changes in the concentration of other electrolytes might have a similar effect. We have no data in the present study on differences in the electrolytes of the umbilical artery and vein. As already indicated Poble and Stewart found that lipemia will increase the speed of clotting. This observation may have a bearing on the present study since Boyd and Wilson reported that blood in the umbilical vein has a higher lipid content than blood in the umbilical artery. Although determinations of fats and lipoids have not been made in these cases, it may be pointed out that in no instance was the plasma from the umbilical vein grossly lipemic.

In spite of these possible explanations, however, the increase in the amount of prothrombin in the umbilical vein may be not only apparent but also real. No one has suggested that prothrombin itself will pass directly from the maternal into the fetal circulation and the

lack of any relationship between the amount of maternal and fetal prothrombin indicates that diffusion from mother to child is unlikely. If such diffusion does not occur therefore, it is possible that prothrombin may actually be formed by the placenta during the period of gestation and the fall in the prothrombin level of some infants following birth may be due in part to the removal of such a source of supply.

#### SUMMARY AND CONCLUSIONS

1. By the Quick method the average plasma prothrombin value of 85 mothers at delivery was greater than the normal controls. The average value of their infants was less than the normal controls.

2. No relationship between the level of prothrombin in mother and baby could be demonstrated. It is unlikely therefore that prothrombin passes directly from mother to fetus.

3. A comparison of the plasma prothrombin levels of the umbilical artery and vein in 35 cases showed that in approximately 70 per cent of these cases the prothrombin value of the vein exceeded that of the artery.

4. If this apparent difference between artery and vein is a real one it is possible that prothrombin may be formed by the placenta.

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#### BIBLIOGRAPHY

- ALDRIDGE, H. J. and STOKES, E. L. R. *J. Nat'l Med.* 1930, 320.
- ANDERSON, W. DEW. LLOYD, J. W. J. and MORTON, R. A. *Surgery* 1930, 8, 802.
- BOYD, E. M. and WILSON, K. M. *J. Clin. Invest.* 1935, 4, 7.
- BRIDGEMAN, K. M., SMITH, H. P. and WARNER, E. D. *Am. J. M. Sc.* 1937, 93, 475.
- HALLMARK, L. M. and SMITH, L. B. *Bull. Johns Hopkins Hosp.* 1930, 45, 18.
- KATO, K. *Am. J. Clin. Pathol.* 1940, 47.
- KATO, K. and FORTCHER, H. G. *J. Am. M. Ass.* 1940, 4, 749.
- NORDEN, R. F. and RICH, A. *Berg. Gynec. & Obst.* 1940, 70, 000.
- OWEN, C. H., HERRING, G. R., ZIFFRIN, S. E. and SMITH, H. P. *Proc. Soc. Exper. Biol. & Med.* 1930, 4, 8.
- POBLE, F. J. and STEWART, J. K. *Am. J. M. Sc.* 1930, 95, 6.
- QUICK, A. J. *J. Am. M. Ass.* 1934, 658.

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- 12 Idem Pennsylvania M J, 1939, 43 125
- 13 Idem Proc Soc Exper Biol & Med, 1939, 42 789
- 14 QUICK, A J, and GROSSMAN, A M Proc Soc Exper Biol & Med, 1939, 41 227
- 15 Idem Am J M Sc, 1940, 199 1
- 16 QUICK, A J, STANLEY BROWN, M, and BANCROFT, F W J Biol Chem, 1935, 109 p lxxiii
- 17 Idem Am J M Sc, 1935, 190 501
- 18 SHETTLES, L B, DELFS, E, and HELLMAN, L M Bull Johns Hopkins Hosp, 1939, 65 419
- 19 SMITH, H P, WARNER, E D, and BRINKHOUS, K M J Exper Med, 1937, 66 801
- 20 WADDELL, W W, JR, and GUERRY, DuP, III J Am M Ass, 1939, 112 2259
- 21 WADDELL, W W, JR, GUERRY, DuP, III, BRAY, W E, and KELLY, O R Proc. Soc Exper Biol & Med, 1939, 40 432
- 22 WARNER, E D J Exper Med, 1938, 68 831
- 23 WARNER, E D, BRINKHOUS, K M, and SMITH, H P Am J Physiol, 1936, 114 667

## RESULTS OF PLASTIC OPERATIONS ON THE RENAL PELVIS AND URETER

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THE answer to the question "Are plastic operations on the renal pelvis and ureter justified?" can be found only in a careful analysis of single case reports with postoperative pyelographic follow-up. The authors, therefore, have studied individually the 32 plastic operations performed at the Mt. Sinai and the Beth Israel Hospitals during the past 3 years. Most of these patients were operated on by the authors, several by the late Dr. Edwin Beer and a few cases by other staff surgeons.

There were 3 operations of necessity the ureter being reimplanted during pyelolithotomy. These cases have been reported in detail elsewhere (7). There were failures in 1: the anastomosis did not heal. The ureter separated from the pelvis and the kidney was subsequently excised. In the second unsuccessful reimplantation the anastomosis healed well. However the stoma was some what narrowed and the kidney which had been grossly infected at the time of operation, gradually became functionless.

These 5 patients, operated on by 5 different surgeons, constitute a special group. In all the kidney was the seat of a calculus with severe infection. The pelvis and ureter were markedly inflamed, and their friability was in every instance considered by the operator the predisposing cause of the avulsion. In 2 of the cases, however, the immediate cause was undue traction on a loop around the ureter. The infiltrated condition of the tissues, as well as the irregularity of the tear made accurate approximation impossible. Despite these difficulties, good functional results were observed shortly after operation and at later pyelographic examinations in 3 of the 5 cases of ureteral avulsion.

The 27 remaining plastic operations were done for hydronephrosis caused by obstruction at the ureteropelvic junction. There were 3 patients in whom a plastic was performed on a solitary kidney. One patient, suffering from bilateral obstruction had both sides operated on.

Relief of the obstruction was the primary object of the surgical treatment in all cases. In 12 in

stances, the cause of the blockage was extrinsic, that is, due to vessels, bands, or adhesions, arising from outside the urinary passages. In 13 cases, the obstruction was due to intrinsic lesions, such as stricture or abnormal insertion of the ureter. In the 2 remaining cases, a portion of the redundant pelvis was resected following pyelolithotomy. The authors have excluded from this study all cases of hydronephrosis due to extrinsic obstruction or to calculus, unless plastic operation on the renal pelvis or ureter was also done.

A dilated kidney and pelvis often will return to relatively normal size if the obstruction is relieved at an early stage. This is especially true in calculous cases in which the obstruction is frequently quite sudden. On the other hand, in some of the larger and more chronic hydronephroses, it was deemed necessary in addition to relieving the obstruction, also to reduce the size of the redundant pelvis by resection or plication.

**Simpler resection.** Resection of the dilated pelvis was the sole plastic procedure in 13 cases. The ureteropelvic obstruction had been adequately relieved by division of aberrant vessels or adhesions or in 2 instances by pyelolithotomy (Table 1). One patient died of accidental mercury poisoning 8 days after operation. This curiously was the only death in the 32 plastic operations. The obstruction was unrelieved in only 1 of the 10 cases in which patients returned to follow-up; nephrectomy was done. The 9 other patients were followed from 5½ months to 12 years; they were well with good renal function. All but one were controlled by excretory or retrograde pyelography and frequently by both.

One of these cases illustrates the value of preliminary nephrostomy drainage in the treatment of grossly infected obstructive hydronephroses.

**CASE 6.** Beth Israel Hospital No. 8,402. This 34 year old man was admitted to the hospital with severe pain in the left loin and high temperature due to purulent hydronephrosis (Fig. 1). A nephrostomy as performed without mobilization of the kidney. The patient's condition improved and 3 weeks later the kidney was exposed and mobilized. The pelvis was still greatly dilated, and there were large aberrant vessels, the ilioaortic branch running over and constricting the ureteropelvic junction. The

From the Urological Surgical Services of the Mt. Sinai and Beth Israel Hospitals.

vessels and bands were divided. The pelvis was opened, a calculus was removed, and an oval flap from the redundant posterior pelvic wall was excised. A nephrostomy tube was reinserted and a second splinting catheter was placed in the ureter and brought out through the cortex adjacent to the nephrostomy. An excretory urogram (Fig. 2), made 3 years after operation, showed excellent function and a much smaller pelvis on the side operated on.

**Pelvic plication.** In 1 case (Beth Israel Hospital No. 104,488) the dilated pelvis was plicated after the obstruction had been adequately relieved by the freeing of ureteropelvic adhesions. A nephropexy was done. A good anatomical and functional result was seen on the excretory urogram 1½ years later.

The pelvis was plicated in 2 other cases, one (Case 31) in association with a side-to-side anastomosis, and the other (Case 27) in addition to section and reimplantation of the ureter. The end result in both of these cases was good. Pelvic plication seems to add little to the risk of operation.

**Plastics at the ureteropelvic junction.** The obstruction was intrinsic in 13 cases, having been caused either by stricture or by abnormal insertion of the ureter. These cases presented a more difficult surgical problem and were treated by a variety of plastic procedures. They are classified under the following headings: (a) Fenger pyeloplasty (2), Y-plastic (3, 11), (b) section of the ureter with reimplantation into the most dependent portion of the pelvis (8, 9), (c) lateral anastomosis of the ureter to the lowermost portion of the pelvis (1).

**Fenger pyeloplasty.** Three Fenger pyeloplasties were done, all before 1932. One patient (Mt. Sinai Hospital No. 299,803) was unrelieved and came to nephrectomy 4 years after operation. The second patient (Beth Israel Hospital No. 37,399) suffered several attacks of acute pyelonephritis and later developed a large perinephric abscess which was drained. Subsequently he passed a small calculus. Despite these complications, however, an excretory urogram made almost 3 years after operation showed good function and a smaller pelvis (Figs. 3 and 4). The third case (Mt. Sinai Hospital No. 344,622) also developed pyelonephritis, but 4 years later showed good function on excretory urography. He still complained of occasional loin pain.

**Y-plastic.** Two Y-plastic operations were done. In the first case (Beth Israel Hospital No. 105,877) there was little, if any, improvement in renal function despite a satisfactory anatomical result. The parenchyma had obviously been irretrievably damaged by long standing obstruction and infection. A conservative plastic operation was at-

TABLE 1—Results

Auvsion of ureter	Cases	Fol lowed	Success ful	Failed	Deaths
Reimplantation	5	5	3	2	0
Hydronephrosis Plastic operations					
Simple resection	13	11	9	1	1
Simple plication	1	1	1	0	0
Fenger	3	3	2	1	0
Y plastic	2	2	1	1	0
Section reimplantation	6	6	4	2	0
Lateral anastomosis	2	2	2	0	0
	27	25	19	5	1

tempted in this case only because the function of the other kidney had also been impaired by adhesions causing ureteropelvic obstruction.<sup>1</sup> In the second case (Beth Israel Hospital No. 116,482) an excretory urogram, made 7 months after operation showed excellent renal function and a small pelvis.<sup>2</sup>

**Results.** The published results of the Fenger operations have been, for the most part, poor (4, 5). Animal experiments indicate that the obstruction is often unrelieved due to buckling of the posterior ureteral wall opposite the plastic suture line. On the other hand, the satisfactory anatomical and functional results in 2 of our cases proves that this is not a constant occurrence. In both of these cases, however, the patients were later operated on for perinephritis. It is interesting to speculate whether the failure to provide free urinary drainage by nephrostomy may have contributed to the high incidence of postoperative perinephric infection.

The Y-plastic, a modification designed to overcome the objections to the Fenger pyeloplasty, resulted in an apparently adequate stoma in our 2 cases. The functional result in one was poor, however, the parenchyma having been irretrievably damaged.

**Section and reimplantation of the ureter.** The authors have observed 6 cases in which the ureter was completely severed and then reimplanted into the dependent portion of the pelvis. These cases were followed for a period of from 1½ to 7½ years after operation. There were 2 failures, one ended in nephrectomy, and the other, a case of giant hydronephrosis in a solitary kidney, was living 4 years later with a permanent nephrostomy. The result in each of the following 4 cases was fairly satisfactory.

**CASE 26.** Mt. Sinai Hospital No. 344,467. This 52 year old woman entered the hospital with high temperature due to a solitary infected hydronephrotic left kidney (Fig. 5). A right nephrectomy had been done for hydronephrosis in 1909. At operation (Dr. Edwin Beer) on October 22, 1932, the left ureter was found stenosed just below its junction with the pelvis. The pelvis was distended with frank pus.

<sup>1</sup> A secondary nephrectomy was recently done at another hospital.

<sup>2</sup> A plain film and excretory urograms made on December 2, 1940 revealed recurrent calculi with considerable hydronephrosis.



The stricture as resected and the cut end of the ureter was reimplanted into the pelvis over a splinting ureteral catheter. A portion of the redundant pelvis as then excised, the opening sutured, and a nephrostomy made.

The patient had a prolonged and stormy convalescence, marked by septic temperature. His recurrent chills. Colon bacilli were recovered in the blood culture. The bacteremia was gradually overcome the patient making slow recovery and leaving the hospital. His months after operation. She has lived fairly comfortably and has attended to her household duties for over 7 years, suffering occasionally from attacks of chills and fever. A retrograde pyelogram (Fig. 6) made in August, 1930, showed considerable dilation of the pelvis and ureter. She as ill when last seen by Dr. W. Henschel early in 1940.

CASE 5. Beth Israel Hospital No. 60,995. This case was reported in some detail (7). At operation on January 8, 1935, the left renal pelvis as found to be very large and distended with straw-colored fluid. The entrance of the ureter into the pelvis was markedly constricted. The ureter was divided below the stricture, and reinserted into the most dependent portion of the pelvis as through a new opening. The ureter as sutured to the pelvis with five plain catgut sutures over Garceau catheter which was brought out through the renal cortex and lumbar wound. The upper end of the ureter as split into flaps which were sutured to the inner surface of the pelvis. A nephrostomy as also made using Dezer catheter.

The immediate postoperative result as good. Indigo carmine appeared from the left pelvis in 5 minutes in good concentration. Excretory and retrograde pyelograms showed, however, some tendency to narrowing at the ureteropelvic junction. The latest excretory urogram, made on March 2, 1936, showed mild degree of hydronephrosis. Its clashing of the calyces and diminished function. Early in 1940, the patient, refusing further ray study stated that she as well.

CASE 7. Beth Israel Hospital No. 60,124. An 8 year old boy as admitted to the hospital. His past and blood in the urine. Pyelography revealed right hydronephrosis with trapping at the ureteropelvic junction. At operation, on November 3, 1934, the pelvis as considerably dilated and there as marked stenosis of the upper catheters of the ureter. The stenosed area as resected. The transversely cut end of the ureter as reimplanted into the pelvis over a splinting No. 5 French ureteral catheter which was brought out through the lower pole next to nephrostomy catheter. The redundant pelvis as closed by plicating sutures.

The immediate postoperative course was uneventful. However, less than a splinting catheter as removed on the twentieth postoperative day the stoma did not function. A retrograde pyelogram, made through the nephrostomy revealed complete obstruction at the ureteropelvic junction. A cystoscope as then introduced into the pelvis through the nephrostomy stoma, but attempts to dilate the stoma from the pelvis downward were unsuccessful. Ten days later however, catheter was easily passed from below up the right ureter into the pelvis. The stoma as then dilated on several occasions. Its indwelling ureteral catheters. The wound healed promptly following removal of the nephrostomy tube on the thirty-sixth postoperative day. This boy has now been perfectly ill for about 4 years after operation. The latest excretory urogram, made on March 14, 1940, showed good function and no progression of the hydronephrosis. The urine was clear.

CASE 8. Mt. Sinai Hospital No. 300,000. This case has recently been reported in detail (6). At operation on September 20, 1932, the left kidney and pelvis were found greatly dilated, and the upper half of the ureter as nearly

completely stenosed. The lower portion of the pelvis which the attached stenosed ureter as resected. The pelvis as closed with fine catgut and No. 8 French soft catheter as inserted through the cortex into the pelvis and ureter as sutured. The ureter as reimplanted into the pelvis.

On the eighteenth postoperative day the tube as pulled upward out of the ureter into the pelvis. Indigo carmine, injected through the nephrostomy tube did not appear in the bladder. On the other hand, catheter as easily passed from below through the anastomotic stoma into the pelvis. It as evident that the anastomosis as obstructed only to the downward passage of fluid. This as repeatedly confirmed by clamping the nephrostomy tube and injecting indigo carmine. Despite several trans-cystoscopic dilations, the efficient function of the stoma could not be established.

Three months after operation, a cystoscope as introduced through the nephrostomy stoma into the renal pelvis. A sickle-shaped fold of mucosa, noted just below the ureteropelvic junction, was thought to be the possible cause of the obstruction. This sickle-like fold as electro-coagulated, and No. 5 French ureteral catheter as passed from below into the pelvis and out through the nephrostomy stoma. The nephrostomy tube was reinserted. Following several trans-cystoscopic dilations, the nephrostomy tube as again clamped off. The stoma as now functioning well. The nephrostomy tube as finally removed 5 months after operation, and the wound as dry within 24 hours.

This patient has been followed for 7 years. During this time, she re-entered the hospital on 6 occasions for cardiovascular disease and increasing hypertension. I 937 splenectomy, sympathectomy, crisis nephrosectomy, lumbar sympathectomy, and renal sympathectomy are done on the right side. There as no lasting improvement. She as admitted to the Montefiore Hospital in 1939 for hypertension, and an excretory urogram showed good function of both kidneys. There are no renal symptoms.

Renal function after operation was fairly good in 4 of the 6 cases of section and reimplantation of the ureter. One of these (Case 26) a woman with an acutely infected solitary hydronephrotic kidney was living comfortably 7 1/2 years after operation. Another (Case 25) followed 4 years, shows some narrowing of the stoma with gradual decline in renal function. Although ultimately satisfactory, the 2 remaining cases developed complete obstruction to the downward flow of urine at the site of anastomosis immediately after removal of the splinting catheter. Pyelography through the nephrostomy sinus in Case 28 revealed a valvular-like mucosal fold, which was thought to be the cause of the obstruction. Following electro-coagulation of this fold and trans-cystoscopic dilatation from below the patency of the stoma was permanently re-established. The function of this kidney was still fairly good 7 years after operation.

In Case 27 the postoperative obstruction of the stoma was overcome by repeated trans-cystoscopic dilatation from below. Renal function was good 3 1/2 years later.

Unrelieved obstruction and infection were responsible for both failures. The first (Case 29



Fig 1 Case 16 Retrograde pyelogram which was taken before operation



Fig 2 Case 16 Excretory urogram 3 years after operation



Fig 3 Case 21 Excretory urogram which was taken before operation



Fig 4 Case 21 Excretory urogram 3 years after Fenger pyeloplasty



Fig. 5. Case 26. Excretory pyelogram before operation in solitary kidney.

(Mt. Sinai Hospital No. 372,441) was a solitary infected giant hydronephrosis due to stricture. The ureter was sectioned and reimplanted but the new stoma failed to function well. This patient was alive almost 4 years later with a permanent nephrostomy. The second unsuccessful case (Case 30, Mt. Sinai Hospital No. 45,327) a 1-year-old boy left the hospital, presumably well, with a healed wound 22 days after operation. Two weeks later the kidney became quite tender and the temperature rose to 104 degrees. The lumbar wound opened spontaneously draining purulent urine. Nephrectomy was done.

The chief difficulty in the cases of section and reimplantation of the ureter was early postoperative obstruction at the site of anastomosis. This occurred in 4 of the 6 cases. Fortunately, however, the obstruction was successfully relieved in 2 cases, in one by electrocoagulation of mucosal



Fig. 6. Case 26. Retrograde pyeloureterogram made 7 1/2 years after section and reimplantation of ureter in solitary kidney.

valve followed by transcystoscopic dilatation, and in the other by dilatation alone. It seems apparent that an effort should be made at the time of operation to prevent the formation of a ureteral fold or cuff at the site of anastomosis. When possible the ureter should be split for a distance of about 1 centimeter into 2 straps (Fig. 7). These are then fastened to the inner aspect of the pelvis by interrupted fine plain catgut sutures. Accurate apposition at suture line is obviously essential. More complicated techniques (13) have been suggested, but are rarely practical.

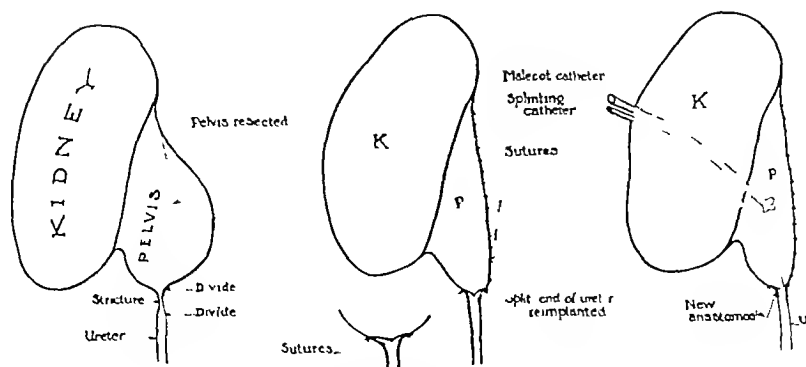


Fig 7 Diagram illustrating section and reimplantation of ureter and resection of pelvis

**Lateral anastomosis** In 2 cases, a side-to-side anastomosis was made between the upper ureter and the most dependent portion of the pelvis. When technically feasible, such a lateral anastomosis has the following advantages over section and reimplantation (13): (1) The vascular supply of the upper ureter is preserved by leaving the ureter attached to the pelvis, (2) there is less interference with peristalsis, (3) a side-to-side anastomotic stoma can be made much larger, thereby lessening the likelihood of early or late stricture.

**CASE 31** Beth Israel Hospital No 75,048. This case has been previously reported in detail (13). At operation on June 20, 1935, the right kidney was greatly dilated. The ureter had a high anterolateral insertion with definite narrowing. A veil of fibrous adhesions extended over the ureteropelvic junction, causing an angulation at the point of insertion of the ureter. A side to side anastomosis was made, over a splinting No. 14 French rubber catheter. A nephrostomy was also done. The redundant pelvis was plicated, following scarification of its external wall. The postoperative course was uneventful, the nephrostomy

tube was removed on tenth postoperative day and splinting catheter on sixteenth postoperative day. Patient has been observed for 5 years with repeated excretory and retrograde pyelograms. Renal function is good, patient is well.

**CASE 32** Beth Israel Hospital No 94,935 (12). This 31 year old man complained of dull pain in the right loin for 10 months and of severe pain the left loin for 4 days. An excretory urogram revealed a large hydronephrosis on the left side and no visualization on the right (Fig 8). A retrograde pyelogram (Fig 9) revealed a huge functionless sac replacing the right kidney. At operation on August 2, 1937, a large left hydronephrosis was found. The ureter had a high lateral insertion, forming an obstructive angle. A side to side anastomosis was made over a splinting No. 8 French ureteral catheter, the catheter being brought out through the cortex. A nephrostomy and nephropexy were also done. The splinting catheter was removed on the twelfth postoperative day. On September 16, 1937, a right nephrectomy was performed. The left nephrostomy tube fell out on September 22, and the wound healed. The patient left the hospital on October 18, voiding well.



Fig 8 Case 32 Pre-operative excretory urogram showing a left hydronephrosis and absent function on the right



Fig 9 Case 32 Pre-operative right retrograde pyelogram

# LESSON OF STUDY

These patients with plastic operations on the ureters and ureter has established the following (1) Free urinary drainage by means of nephrostomy (2) splitting of anastomosis (3) means of a catheter (3) accurate approximation of sutured parts.

Free drainage is prime requisite in the treatment of urinary infection from which most of these patients suffer. A nephrostomy should, therefore, be performed in all cases in which any extensive pelvic or ureteropelvic plastic procedure is done. The tube acts as a safety valve preventing undue internal tension on the suture lines. In addition, it may be used for the instillation of bactericidal solution.

Prolonged drainage is often desirable. The anastomosis is put to a practical functional test by clamping off the nephrostomy tube for several days before its final removal. Should the anastomosis fail to function satisfactorily the tube is again allowed to drain. This gives additional opportunity for edema and infection to subside and for trans cystoscopic dilatation of the anastomosis. In 2 cases (Cases 27 and 28), a cystoscope was introduced through the nephrostomy sinus for direct visualization of the pelvis and site of anastomosis. In one of these, endopelvic electrocoagulation of a valve-like mucosal fold was followed by the permanent re-establishment of patency of the ureter.

The authors believe that the nephrostomy tube should be left in place for at least 2 weeks and often for a much longer time. It should be removed only after the adequacy of the anastomotic opening has been proved and when the infection has been well controlled. The administration of drugs, such as sulfanilamide and sulfapyridine is frequently effective, especially after removal of the tube.

After operation made 3 years after skin  
urinary kidney Patient still  
made operation 23 hours later his severe pain in the  
lower back and anuria. At cystoscopy the bladder  
was empty and an impassable obstruction was en-  
countered at the ureter 4 centimeters above its orifice.  
Nephrostomy was immediately performed and the  
urine was again voidable. This obstruction  
was probably due to small non-opaque calculus,  
however, was not recovered. The ureteropelvic  
anastomosis was divided a number of times from below. The  
nephrostomy tube was then clamped off and the patient  
voided normally. A clamped-off nephrostomy tube was  
used as safety valve for about year. The tube was  
removed and the wound healed promptly. The  
urine cultures were sterile. Bacillus coli,  
Bacillus pyocyaneus, and Bacillus lactic aerogenes. After  
course of sulfanilamide, urine became sterile. Blood non-  
protein nitrogen was 38 milligrams. An excretory urogram,  
June 1930 (Fig. 1) showed good function of left kidney.  
Patient still voiding 3 years after operation.

The end result in the 2 cases of late  
results was satisfactory. In Case 3  
pelvic plication was also done. The func-  
tion of the kidney operated on was good after  
the second case, the anastomosis in  
urinary kidney. This patient is well  
with adequate renal function 3 years after operation.

may precipitate calculous formation when in contact with urine

#### SUMMARY

1 The results of 32 plastic operations on the renal pelvis and ureter have been reported and analyzed. In 5 cases, the ureter was reimplanted in the renal pelvis following accidental avulsion. The 27 remaining plastic operations were done for hydronephrosis due to obstruction at the ureteropelvic junction.

2 Relief of obstruction was the primary object of the surgical treatment of hydronephrosis. In some cases, the dilated pelvis was also resected or plicated.

3 The various types of plastic operations employed are discussed and evaluated, and illustrative cases are recorded in some detail.

4 Early postoperative obstruction at the site of anastomosis was encountered in 4 of 6 cases of section and reimplantation, and in 2 of 5 cases of reimplantation following accidental avulsion.

5 Transcystoscopic dilatation was effective in several cases in overcoming early postoperative obstruction.

6 Direct pyeloscopy through the nephrostomy sinus was done in 2 cases. In 1 instance, the

patency of the stoma was re-established, following electrocoagulation of a valve-like mucosal fold near the site of anastomosis.

7 Late stricture was observed in 1 case of section and reimplantation, 1 case of reimplantation following avulsion, and 1 case of Fenger pyeloplasty.

8 Side-to-side anastomosis of the ureter and pelvis, when feasible, appears preferable to section and reimplantation.

#### REFERENCES

- 1 ALBARRAN, J. *Médecine opératoire des voies urinaires*. Pp 222-226. Paris: Masson, 1909.
- 2 FENCER, C. *J Am M Ass*, 1894, 22: 335, 840.
- 3 FOLEY, F E B. *J Urol*, 1935, 34: 612.
- 4 HENLINE, R B. *J Urol*, 1935, 34: 584.
- 5 HERBST, R H, and POLKEY, H J. *J Urol*, 1930, 23: 23.
- 6 HYMAN, A, and LEITER, H. *J Mt Sinai Hosp*. In press.
- 7 HYMAN, A, and WILHELM, S F. *J Urol*, 1940, 43: 52.
- 8 KUESTER, E. *Die Chirurgie der Nieren*. Pp 503-508. Stuttgart: Ferd Enke, 1896-1902.
- 9 Idem. *Arch f klin Chir*, 1892, 44: 850.
- 10 LUBASH, S. *J Urol*, 1935, 34: 222.
- 11 SCHWYZER, A. *Schweiz med Wchschr*, 1931, 12: 1185.
- 12 WILHELM, S F. Discussion. American Urological Association, Buffalo, 1940. *J Urol*. In press.
- 13 WILHELM, S F, and BLINICK, G. *Am J Surg*, 1937, 35: 90.



Fig. Excretory urogram made 3½ years after side to-side anastomosis. Solitary kidney. Patient, ell.

If readmitted 4 hours later with severe pain in the left loin, high fever and anuria. At cystoscopy the bladder was empty and an impassable obstruction was encountered in the left ureter 4 centimeters above its orifice. A nephrostomy was immediately performed and 1 week later the patient was again able to void. This obstructive episode was probably due to a small non-opaque calculus, which, however, was not recovered. The ureteropelvic stoma was dilated a number of times from below. The nephrostomy tube was then clamped off and the patient voided normally. A clamped-off nephrostomy tube was left in situ as a safety valve for about 1 year. The tube was finally removed and the wound healed promptly. The urine cultures at various times had shown *Bacillus coli*, *Bacillus pyocyaneus*, and *Bacillus lactis aerogenes*. After course of sulfanilamide urine became sterile. Blood non-protein nitrogen was 35 milligrams. An excretory urogram, June, 1940 (Fig. 1) showed good function of left kidney. Patient well and working 3 years after operation.

The end-result in the 2 cases of lateral anastomosis was satisfactory. In Case 31 in which a pelvic plication was also done the function of the kidney operated on was good after 5 years. In the second case, the anastomosis was made on a solitary kidney. This patient is well with adequate renal function 3 years after operation.

#### ANALYSIS OF STUDY

Increased experience with plastic operations on the renal pelvis and ureter has established the following principles: (1) Free urinary drainage by means of nephrostomy; (2) splinting of anastomosed parts by means of a catheter; (3) accurate apposition of sutured parts.

**Nephrostomy.** Free drainage is a prime requisite in the treatment of urinary infection from which most of these patients suffer. A nephrostomy should, therefore, be performed in all cases in which any extensive pelvic or ureteropelvic plastic procedure is done. The tube acts as a safety valve preventing undue internal tension on the suture lines. In addition, it may be used for the instillation of bactericidal solution.

Prolonged drainage is often desirable. The anastomosis is put to a practical functional test by clamping off the nephrostomy tube for several days before its final removal. Should the anastomosis fail to function satisfactorily the tube is again allowed to drain. This gives additional opportunity for edema and infection to subside and for transcathectic dilatation of the stoma. In 2 cases (Cases 27 and 28), cystoscopy was introduced through the nephrostomy sinus for direct visualization of the pelvis and site of anastomosis. In one of these endopelvic electrocoagulation of a valve-like mucosal fold was followed by the permanent re-establishment of patency of the stoma.

The authors believe that the nephrostomy tube should be left in place for at least 2 weeks and often for a much longer time. It should be removed only after the adequacy of the anastomotic opening has been proved and when the infection has been well controlled. The administration of drugs, such as sulfanilamide and sulfapyridine is frequently effective especially after removal of the tube.

**The splinting catheter.** A straight ureteral catheter is inserted into the ureter for a distance of about 10 centimeters below the site of anastomosis and brought out through the renal pelvis and cortex. It serves the double purpose of immobilizing the anastomosed parts and maintaining the new opening. The splinting catheter should be left in place for at least 10 days since its early removal may result in stricture or occlusion of the stoma.

**Accurate apposition.** Accurate suture of the mucosa and the muscularis in separate layers is recommended when possible by means of fine interrupted plain catgut sutures for the mucosa and fine interrupted chromic sutures for the outer layers. Non-absorbable suture materials are contra-indicated since they act as foreign bodies and

may precipitate calculous formation when in contact with urine

#### SUMMARY

1 The results of 32 plastic operations on the renal pelvis and ureter have been reported and analyzed. In 5 cases, the ureter was reimplanted in the renal pelvis following accidental avulsion. The 27 remaining plastic operations were done for hydronephrosis due to obstruction at the ureteropelvic junction.

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#### REFERENCES

- 1 ALBARRAN, J. *Médecine opératoire des voies urinaires*. Pp 222-226. Paris: Masson, 1909.
- 2 FENCER, C. *J Am M Ass*, 1894, 22: 335, 840.
- 3 FOLEY, F E B. *J Urol*, 1935, 34: 612.
- 4 HENLINE, R B. *J Urol*, 1935, 34: 584.
- 5 HERBST, R H, and POLKEY, H J. *J Urol*, 1930, 23: 23.
- 6 HYMAN, A, and LEITER, H. *J Mt Sinai Hosp*. In press.
- 7 HYMAN, A, and WILHELM, S F. *J Urol*, 1940, 43: 52.
- 8 KUESTER, E. *Die Chirurgie der Nieren*. Pp 503-508. Stuttgart: Ferd Enke, 1896-1902.
- 9 Idem. *Arch f klin Chir*, 1892, 44: 850.
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- 11 SCHWYZER, A. *Schweiz med Wchschr*, 1931, 12: 1185.
- 12 WILHELM, S F. *Discussion American Urological Association*, Buffalo, 1940. *J Urol*. In press.
- 13 WILHELM, S F, and BLINICK, G. *Am J Surg*, 1937, 35: 90.



# USE OF THE IAG SCREW FOR INTERNAL FIXATION OF INTERTROCHANTERIC FRACTURES OF THE FEMUR

MELVIN A. CASBERG, M.D., St. Louis, Missouri

FROM the standpoint of medical literature one is impressed by the obscurity into which extracapsular fractures of the femur have fallen. Recent progress in the therapy of intracapsular fractures has so absorbed medical interests that there is a tendency to neglect an adjacent fracture of equal importance. Prior to Smith-Petersen's contribution to the therapy of fractures of the femoral neck, the capsule played an important rôle as a landmark of prognostic value. This factor was first emphasized by Sir Astley Cooper who distinguished between intracapsular and extracapsular fractures and defined the poor prognosis of the former and the much better prognosis of the latter. True as these facts are they have in many instances led to a certain therapeutic fallacy in the assumption that treatment of extracapsular fractures is relatively unimportant because union is inevitable. Though this assumed truism is correct in part it is better clarified by the additional statement that union is inevitable in those patients who survive sufficient period of time to permit such a process.

The study of mortality statistics in intertrochanteric fractures is rather disturbing and is prone to produce a somewhat pessimistic attitude. In the St. Louis City Hospital during 1937 the mortality rate for extracapsular fractures was

From the Department of Surgery, St. Louis City Hospital.

approximately 40 per cent, while for intracapsular fractures it was 28 per cent (9). This difference is made possible by two definite factors: first, intertrochanteric fractures in general are associated with more shock and with greater trauma to the soft tissues as well as to the bone; second, the age of those suffering extracapsular fractures averages from 3 to 10 years above that of those with fractures of the femoral neck (11, 12). Intertrochanteric fractures usually show considerable trauma of the vastus lateralis, rectus femoris, and tensor fascia lata muscles with the extravasation of blood into the muscle bodies and even the presence of large intramuscular hematomas. This excessive tissue damage is the exception in fractures of the femoral neck where the trauma is localized fairly well within the joint capsule.

In recapitulation it might be stated briefly that to a certain extent the therapeutic problem presented by intracapsular fractures is that of union, whereas, in extracapsular fractures the problem of union is secondary to that of the maintenance of life.

In 1871 Hodgen described a swinging double inclined plane splint that is still employed by some surgeons in the therapy of extracapsular fractures. Though this method of treatment has produced excellent anatomical results in our hands, it requires the patient to remain in bed during the



Fig. 1. a, Roentgenograms taken on admission of W. W. (Case 1), male, aged 5 years. Routine operation as performed. Complete reduction and fixation are shown in b and c. Patient, as permitted to be up on bed chair on twelfth day, walked with the aid of crutches on the eighteenth day and bore weight with the aid of

crutches, 5 weeks after operation. Eight weeks after operation the crutches were discarded and the patient walked using crutches. d, taken 3 months after operation shows the union of callus covering the tail of the screw. Patient followed for 3 months and has free motion of his injured hip. (Operation August, 1930.)

interim of immobilization, which averages about 10 weeks. This prolonged period of recumbency is a dangerous factor, especially in the aged. Various methods of fixation have been devised in order to permit the patient greater mobility. One of the better known is the well-leg traction splint described by Roger Anderson. With this type of fixation the patient may be permitted a certain degree of mobilization almost immediately following reduction. Utilization of this principle in the St. Louis City Hospital (14) during the year 1938 to 1939 improved the mortality statistics slightly more than 10 per cent. Though there are certain disadvantages, the chief of which is the difficulty in rehabilitation due to pain in the joints, well-leg traction affords good fixation for a large percentage of intertrochanteric and subtrochanteric fractures.

Key, in an effort to reduce the high mortality rate in trochanteric fractures of the femur, resorted to internal fixation of these by the insertion of the Smith-Petersen nail. This method did not prove entirely satisfactory, for Key states, "In the beginning we had hoped for a method which would fix these trochanteric fractures to the same degree and afford the same freedom from casts and splints and permit the patient to be gotten out of bed soon after the operation, as is the case in fractures through the neck of the femur which have been nailed. However, it seems evident that this is not possible, because of the tendency to comminution and of the rather wide variation in the type of fracture encountered."



Fig 2 Photograph (Case 1) taken 3 weeks after operation to demonstrate free motion of the hip

#### THE LAG SCREW

It is not the purpose of this paper to discuss the advantages or disadvantages of the flanged nail, pin, or screws in the fixation of femoral neck fractures, for, in the hands of their individual masters each has proved successful. It is the purpose of this paper, however, to discuss the Leydig and Brookes (10) modification of the Henderson lag screw as a method of fixation of certain selected intertrochanteric fractures. This lag screw cannot be used indiscriminately on all extracapsular fractures and the cases must be selected carefully from the standpoint of the type of fracture. Subtrochanteric and markedly comminuted intertrochanteric fractures do not lend themselves to this type of fixation, for it is essential to have a

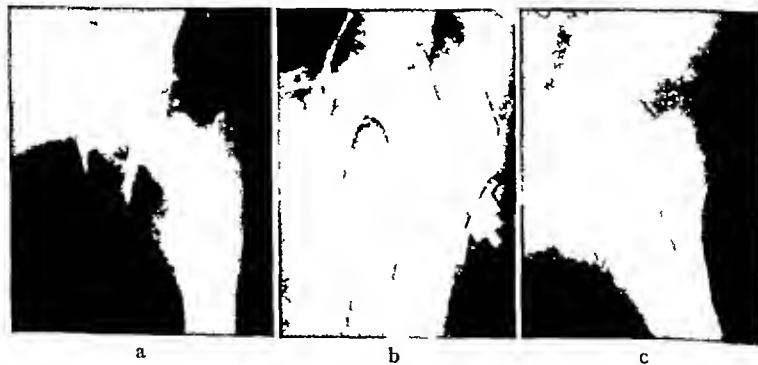


Fig 3 a, Roentgenogram taken on admission of M. S. (Case 2), female, aged 69 years. b and c were taken immediately after operation. The patient was up in a wheel chair on the fourth day, and was walking with the aid of crutches just 2 weeks after operation. Weight bearing was commenced 5 weeks after operation and the crutches were discarded 5 weeks later, though at times one crutch was used when the patient had to walk more than usual. Motion at the hip was free and painless. Five months after operation the patient was using a cane but was able to get about quite well. (Operation February, 1940)



Fig. 4. a, Roentgenogram taken on admission of W. W. (Case 5), male, aged 75 years. Operation was performed in the routine manner and postreduction plates, b and c, show position of the lag screw. (Operation February 1940)

portion of the greater trochanter attached to the distal fragment as a point of purchase for the flange of the screw.

The advantages of this lag screw in fixation are chiefly those of early mobilization of the patient. This factor entails not only the reduction of the mortality rate and a great decrease in the period of hospitalization, but also added comfort and an improvement in the morale of the patient who is not encumbered with casts or traction apparatus of any sort.



Fig. 5. Case 5. Patient up in bed chair on fourth day showing type of dressing; the ACE bandage has long been removed.

The instrument of fixation is made up of a unit of three separate parts: the lag screw which is inserted well into the femoral head; a rectangular flange which grasps the lateral surface of the greater trochanter and femoral shaft; and a nut, which when applied to the tail of the screw over the flange impacts and immobilizes the fractured fragments. The shaft of the screw measuring 4 inches in length terminates in a head made up of a wide wood-screw (twist of six turns) which penetrates and grasps the trabecular bone of the femoral head. The threaded tail of this instrument contains a slot which is adapted to receive the brace during its insertion and also to lock the flange to prevent its rotation after insertion. The rectangular flange measuring five-eighths of an inch wide by two and a quarter inches long, is sufficiently large to afford a distribution of the lines of force over a wide surface of bone along the lateral portion of the greater trochanter and femoral shaft. In addition to this armamentarium a drill is needed to penetrate the cortex of the bone prior to insertion of the screw and a wrench for the turning of the nut.

#### THE TECHNIQUE OF OPERATION

One hundred milligrams of novocain is injected to produce spinal anesthesia, and an arthrotomy is performed after the method described by Cubbins and his co-workers. The skin incision extends from a point approximately 1 inch inferior to the anterior iliac spine, distally in vertical plane about 8 inches, and then curves laterally a distance of some 5 inches. A cleavage plane is then sought lying between the tensor fascia lata on the lateral side and the sartorius on the medial side. The insertion of the former muscle into the iliofemoral tract of the fascia lata is then divided at

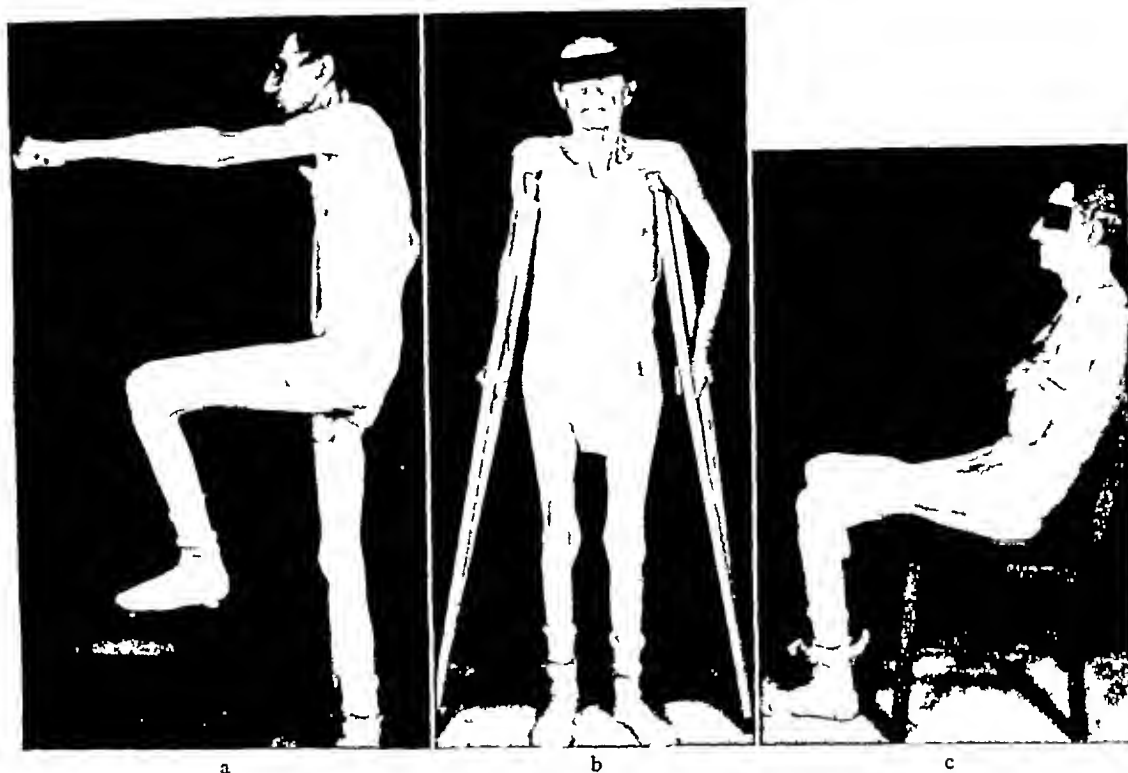


Fig 6 Case 3 Crutches used 2 weeks after operation, without weight bearing Three weeks after operation there is complete and painless motion of the involved hip, a, b, c

Crutches were discarded 8 weeks after operation and cane was used for 2 weeks When last seen the patient was walking well and without a limp

right angles so that the skin and the underlying muscle can be turned laterally as a flap By the retraction of the rectus femoris and sartorius muscles medially the joint capsule is readily identified and a cruciate incision is made to expose the femoral neck and head Very little bleeding is encountered if the branches of the lateral femoral circumflex vessels are identified and ligated as they pass through the operative field The vastus lateralis muscle originating from the lateral surface and base of the greater trochanter is then split in a vertical plane, and a mastoid retractor is placed so as to expose the shaft of the femur in this region

When the fracture site has been exposed and reduced by the Leadbetter maneuver, a drill hole is made from the lateral surface of the femoral shaft about 1 inch distal to the base of the greater trochanter, extending through the cortex and partially into the head of the femur After the desired length is determined by direct measurement, the lag screw is inserted under visual surveillance, the exposed femoral head and neck being used as landmarks The flange is then applied and the

nut is tightened so as to reduce and hold the intertrochanteric fracture firmly It is important that the flange be bent to fit the lateral contour of the bone without the interposition of soft tissues, for, should this be neglected, necrosis of the crushed soft tissues will result in the loosening of the screw

The only deep structures which require suturing are the joint capsule and the insertion of the tensor fascia lata muscle The remaining split muscle planes approximate themselves quite readily without fixation Black silk is used throughout as a suture material Before the closing of the wound, about 10 grams of sulfanilamide powder are sprinkled into the joint cavity and depths of the wound An ACE bandage is applied over the sterile dressing as a hip spica in an effort to eliminate any possible dead space The operative procedure consumes from 30 minutes to 1 hour depending upon the type of fracture, the ease of reduction, and the rapidity of fixation Spinal anesthesia affords very good relaxation which is an important factor in approximation of the fragments In our experience the operation has not seemed to cause shock and the patients in retro-



Fig. 4. a, Roentgenogram taken on admission of W. W. (Case 3), male, aged 73 years. Operation as performed in the routine manner and postreduction plates b and c, show position of the lag screw. (Operation February 9, 50)

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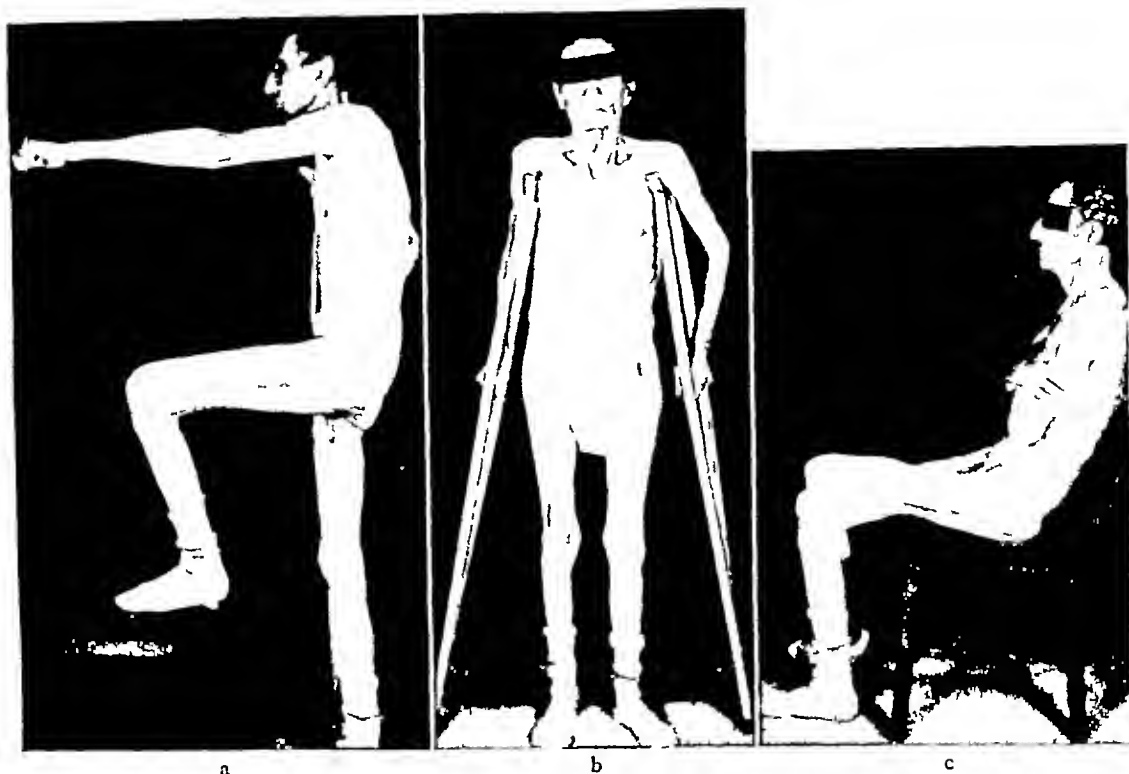


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Fig. 7. a, Roentgenogram taken on admission of E. C. (Case 4) male aged 53 years, showing considerable comminution of intertrochanteric region. Routine operation with insertion of lag screw as performed under direct vision. Results are shown in b and c. The patient is up on his feet four on the tenth day and is walking with the aid of crutches three weeks after operation. Three weeks later weight bearing is permitted and he is walking without support. Motion is free except for abduction which is somewhat limited.

spect do not complain of discomfort resultant from this procedure.

The postoperative program followed is to have the patient propped up in bed 12 hours after the operation. The lower extremities are not encumbered by any traction apparatus and are left to roll freely about in bed. By the end of the second week, and in most cases within the first week, the patient is up in a wheel chair for short periods daily. Approximately 2 to 3 weeks after operation the patient is walking with the aid of crutches without weight bearing and after a period of 5 to 6 weeks weight bearing is permitted. The crutches are discarded in about 8 to 9 weeks and a cane is used if the patient so desires. Thus the patient with an intertrochanteric fracture is rehabilitated within a period of about 2 months.

#### EVALUATION

As in the case of the Smith-Petersen nail insertion of the lag screw may be accomplished in one of two ways either through a small lateral incision over the base of the greater trochanter in which case the progress of the screw is determined by repeated roentgenograms, or by direct vision through exposure of the fracture site and the femoral neck and head. The lag screw was primarily devised for insertion by the former method, but for reasons to be discussed, these cases herein presented were reduced and immobilized by the latter technique.

Brittain in discussing the disadvantages of the open operation and insertion of the Smith-Petersen nail under direct vision raised the following objections: (1) Complete reduction by means of open operation is by no means certain. (2) the operation is a difficult one and undoubtedly carries a certain mortality. (3) radiology on the oper-

ating table when there is a large incision, undoubtedly exposes the patient more to risks of infection than when the incision is confined to one-half inch. (4) there is frequently a certain amount of fibrosis associated with the opening of the capsule of the hip joint with resultant limitation of motion.

In the St. Louis City Hospital prior to August, 1939, the vast majority of the fractures of the femoral neck had been nailed by the closed method, but since that time most of the fixations have been accomplished by the open operation. This latter exposure afforded such an excellent view of the fracture site that it was adopted for the introduction of the lag screw as well. Though the points raised by Brittain refer specifically to fixation of fractures of the femoral neck by the Smith-Petersen nail, the same objections might well be raised to the open fixation of intertrochanteric fractures with the lag screw. Granted that the technique of open operation is somewhat more difficult, this factor should not be used as an excuse for its rejection because actual visualization of the fracture site affords not only a better opportunity for exact reduction and fixation but also permits testing of the solidarity of the immobilized fragments. This last is accomplished by motion of the thigh while observing the point of fracture. There is no need for radiological apparatus in the operating room for the course of the screw can be determined by direct measurement of the exposed femoral head and neck. Thus there is need for only two sets of roentgenograms, one before operation to diagnose the type of fracture and one after the operation to verify the success of fixation.

One of the hazards of orthopedic surgery has been infection and there are few fields of surgery

in which this complication can cause greater havoc Jensen and his co-workers have presented a series of compound fractures in which the local implantation of sulfanilamide greatly reduced the percentage of wound infections Stimulated by this report a policy was adopted of implanting about 10 grams of sulfanilamide powder in the operative wound, and this simple but effective measure has proved to be of definite value in the prevention of infection

It may appear to some that arthrotomy is an unnecessary procedure because intertrochanteric fractures are extracapsular in position, yet, in order to direct the screw accurately and determine the depth of insertion, the femoral neck and head must be exposed Experience both with the lag screw and Smith-Petersen nail has given no reasons to indicate that arthrotomy has resulted in a lack of free motion which might be ascribed to fibrosis of the joint capsule

The limitations of this method of fixation are well recognized, for not every type of trochanteric fracture can be immobilized by the lag screw In order to compete with extracapsular fractures the surgeon must be familiar with a varied armamentarium which should also include such factors as the Hodgen splint, varieties of the Whitman cast, and well leg traction Each case may then be investigated from the standpoint of the type of fracture, age, economics, etc., and the final verdict thus determined Since union of intertrochanteric fractures is the rule it is possible to determine the end-results at a much earlier date than is the case in femoral neck fractures, in which bone absorption and nonunion are encountered as complications It is not necessary to remove the lag screw after union has occurred, though this is readily accomplished through a small incision over the tail of the screw In certain cases the projecting tail of the screw is covered with a bone callus which tends to eliminate this as a possible source of irritation

#### CONCLUSIONS

1 The mortality rate in intertrochanteric fractures of the femur is greater than that in fractures of the femoral neck

2 Recent medical literature stresses the therapy of intracapsular fractures to the relative neglect of trochanteric fractures

3 Four cases of intertrochanteric fractures of the femur are presented in which the lag screw was used as a method of internal fixation

4 It is believed that in selected cases this procedure will result not only in a reduction of the mortality rate but also in a much shorter period of hospitalization

5 It would appear that best fixation is obtained by open reduction and insertion of the lag screw under direct vision

#### BIBLIOGRAPHY

- 1 ANDERSON, R A A new method for treating fractures utilizing the well leg for countertraction *Surg, Gynec & Obst*, 1932, 54 207
- 2 BRITTAN, H A Insertion of the Smith Petersen nail into the femoral neck *Brit M J*, 1936, 1 838-840
- 3 CUBBINS, W R, CALLAHAN, J J, and SCUDERI, C S Fractures of the neck of the femur *Surg, Gynec & Obst*, 1939, 68 87-94
- 4 HENDERSON, M S Internal fixation of fractures of the neck of the femur *Arch Surg*, 1937, 35 419-430
- 5 HODGEN, J T On fractures, lecture 9 *St Louis M & S J*, 1871, 8 228
- 6 JENSEN, N K, JOHNSRUD, L W, and NELSON, M C The local implantation of sulfanilamide in compound fractures *Surgery*, 1939, 6 1-12
- 7 KEY, J A Internal fixation of trochanteric fractures of the femur *Surgery*, 1939, 6 13-23
- 8 LEADBETTER, G W Treatment for fracture of neck of femur *J Bone & Joint Surg*, 1933, 15 931-940
- 9 LEYDIG, S M Fractures of the neck of the femur treated with the Smith Petersen nail *Surg, Gynec & Obst*, 1939, 68 713-717
- 10 LEYDIG, S M, and BROOKES, T P Treatment of per-trochanteric fracture of the femur with a lag bolt *J Missouri State M Ass*, 1940, 37 354-357
- 11 MOORE, A T Fracture of the hip joint *Surg, Gynec & Obst*, 1937, 64 420-436
- 12 ROWLETTE, A P, HASLEM, J R, SIEGERT, R B, MORRIS, H D, and KEY, J A Results obtained by subcutaneous pinning of fractures through the neck of the femur *J Am M Ass*, 1936, 107 1610-1614
- 13 SMITH-PETERSEN, M N, CAVE, E F, and VANG-ORDER, G W Intra-capsular fractures of the neck of the femur, treatment by internal fixation *Arch Surg* 1931, 23 715-759
- 14 WEINFR, DAVID Personal communication to the author Data to be published



# COMBINED TRACTION COMPRESSION METHOD FOR THE TREATMENT OF BICONDYLAR FRACTURES OF THE TIBIA

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**C**OMBINED traction and compression are required for the satisfactory reduction of bicondylar fractures of the tibia. These injuries are produced by a force which drives the hard cortical shaft of the tibia into the soft expanded cancellous portion of the tibial plateau, resulting in a splitting, separation and depression of the condyles. It is clear that any satisfactory method of treatment must correct the upward thrust of the tibial shaft as well as reduce the lateral displacement and depression of the tibial condyles. Traction alone without compression of the condyles is insufficient, compression without traction will result in unsatisfactory alignment of the fragments. A combination of both traction and compression is necessary. Moreover these forces must be applied in such a manner that they can be maintained until the fracture is firmly united. To apply compression by means of a carpenter's clamp and then, of necessity to release it will frequently result in a recurrence of the deformity. To maintain traction by means of a casting is impossible.

It is the purpose of this paper to present a simple method of applying continuous traction and compression for the reduction and fixation of displaced bicondylar fractures of the tibia. The traction is obtained by means of a Kirschner wire which is inserted through the calcaneus; the compression, by sleeved wire (s) inserted through the tibial condyles.

The following case report demonstrates the application of this method.

## CASE REPORT

*J. J. male, aged 27 years, as admitted to Kirschner Hospital on June 4, 1939. He stated that while riding bicycle the front wheel suddenly caught in its frame and he was thrown forward striking his right leg against the curb.*

*Examination revealed swollen, tender, discolored right knee. There was evident indenting of the tibial plateau and the lateral condyle and head of the fibula were abnormally prominent. There was moderate valgus deformity and slight external rotation of the leg. The knee joint was unstable.*

*His range of anteroposterior and lateral mobility.*

*Roentgenogram (Fig. 1) showed comminuted bicondylar fracture of the tibia. It showed outward displacement of the lateral and depression of the medial condyle.*

*From the Fracture Service of Kirschner Hospital.  
Read before the Surgical Section of the New York Academy of Medicine, October 4, 1940.*

*Russell traction as applied to the right leg for 6 days. His resulting improvement in the alignment of the fragments but with no change in the outward displacement of the lateral condyle or the depression of the medial condyle. It was evident that compression of the condyles, as well as traction in the long axis of the leg, was necessary.*

*Combined continuous compression and traction as applied on June 5, 7 days following the injury. The compression sleeve used consists of three parts: (1) Kirschner wire of medium diameter to which is added fixed metal head and washer; (2) metal sleeve which slips over the wire; and (3) threaded collar. It is set screw and nut.*

*Technique: Under nitrous-oxide-oxygen anesthesia, Kirschner wire as inserted through the calcaneus and traction as applied to the leg. An incision one-half inch in length was made over the lateral tibial condyle midway between its anteroposterior diameter and 5 centimeters below its articular surface. The sleeved wire with the fixed head and washer as then inserted through the upper end of the tibia, emerging on the inner side of the knee through the medial condyle; the washer placed against the pericapsule of the lateral condyle. A condylar incision as made at the point of exit and the metal sleeve slipped over the wire and brought into contact with the medial condyle. The threaded collar as then placed on the wire and fixed by means of its set screw. The wire as turned, and as it approached the medial condyle compression as exerted through the sleeve, forcing the condyles together.*

*Roentgenogram (Fig. 2) showed marked improvement in the position of the fragments. The leg as placed on Boehler frame. It showed pounds of traction applied through the calcaneus and its compression maintained by action of the sleeve (Fig. 3).*

*After-care: Baling and massage. His quadriceps exercises were begun early. The compression force as unchanged but the traction as reduced to 5 pounds after 5 weeks. Seven weeks after reduction, under local anesthesia, the compression wire as removed from the upper end of the tibia and the Kirschner wire as withdrawn from the calcaneus. A plaster casting as applied from the toes to the mid thigh, with the knee in 5 degrees of flexion. The patient as allowed up on crutches and discharged 4 days later. The casting as bivalved 9 weeks after reduction and removed daily for massage and active knee motion. The incisions: the upper end of the tibia had healed per primam. Three months after reduction, a walking caliper brace as applied. Unsupported weight-bearing as allowed 6 months after the injury. Examination of the patient in May 1940, 10 months after reduction, revealed stable, painless knee with complete extension and 35 degrees of flexion (Figs. 4 and 5). There was no anteroposterior motion of the knee joint and only slight lateral mobility. Roentgenograms (Fig. 6) showed firm healing of the fracture.*

The method described makes possible the continuous action of the two forces required. Continuous compression could be obtained by bolt but

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Fig 1

Fig 2

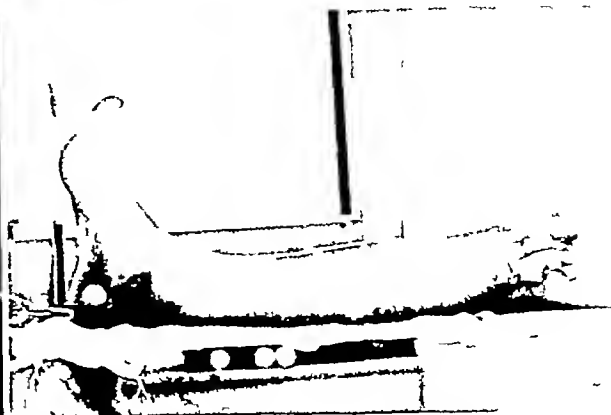


Fig 3

Fig 1 Before reduction Note marked outward displacement of lateral condyle and depression of medial condyle

Fig 2 After reduction

Fig 3 Showing compression sleeve in tibial condyles and Kirschner wire through calcaneus



Fig 4

Fig 5

Fig 6

Fig 4 Appearance of leg 11 months after reduction

Fig 5 Degree of flexion present 11 months after reduction

Fig 6 Roentgenogram 11 months after reduction

the sleeved-wire has the advantage of simplicity of insertion and removal with minimal trauma to the cancellous bone

The points chosen for the insertion and exit of the compression wire will vary with different displacements and should be determined after careful study of the roentgenograms. In some cases the wire will be introduced 1 centimeter below the articular surface, in others a position several centimeters lower will effect the best compression. As the normal landmarks about the knee are often obliterated by soft part swelling, it is advisable to place a marker across the upper end of the tibia in what is considered the desired position and to take

an anteroposterior roentgenogram. The correct position in the longitudinal plane for the insertion of the wire can be easily determined from the position of the marker. In the vertical plane, the wire should be introduced into the center of the tibia, a point easily selected by means of palpation.

Arthrotomy is indicated in many badly displaced bicondylar fractures because of severe injury to the semilunar cartilages and lateral ligaments. Because the methods for reduction and fixation of the bony fragments at open operation have not always been successful, it is suggested that if arthrotomy is performed, the displaced

condyles may be reduced and fixed by the combined traction-compression method where is here described.

#### SUMMARY

1. A method combining continuous traction and compression is reported.

2. The value of the combined traction-compression principle in the reduction and fixation of

a bicondylar fracture of the tibia is demonstrated.

3. Traction is obtained through a Kirschner wire in the calcaneus.

4. Compression is applied by means of a compression sleeve which is inserted through the condyles.

#### REFERENCE

Whipple T. A sleeve-wire method of fixation of fractures. *J Bone & Joint Surg.* 39. 9-4

# RELATION OF PYELONEPHRITIS TO TOXEMIAS OF PREGNANCY

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**D**URING recent years Peters (8-11) has been foremost in presenting data which might suggest pyelonephritis as a possible cause of toxemia of pregnancy, the general term describing certain complications which occur during gestation, whose symptoms at times include headache, visual disturbances, irritability, nausea, vomiting, epigastric pain, rapid gain of weight, and, perhaps, convulsions. Frequent clinical findings are edema, hypertension, and albuminuria. It is evident that many of the signs and symptoms of toxemia are also common in various types of renal disease. So many theories of the cause of toxemia have been advocated that it is evident that no one yet knows the answer to this problem.

General agreement has existed during the past few years that vascular change (4) is the basic pathological conception. Pathological changes in toxemia, as in essential hypertension, are found more commonly in the kidneys than in other organs of the body (3). While the changes accompanying these troubles in the kidney are somewhat variable in both their extent and their variety, Fahr, Bell, Baird and Dunn have reported thickening of the capillary walls of the glomeruli due particularly to thickening of the basement membrane in the capillary tufts. The increase in bulk produced by the thickened connective tissue membrane contributed to the obstructive effect in the capillary.

Although it is not certain what initiates this clinical or pathological condition in pregnant women without previous vasculorenal disease, the symptoms which the toxemias and certain renal diseases possess in common have led to a broader conception of the problem. The more comprehensive point of view can be visualized if one compares the classification of toxemias today with that of 20 years ago (14). At that time nephritic toxemia, pre-eclamptic toxemia, and eclampsia formed the only subdivisions of this subject. Contrast today's proposed classification (Table I) recently offered by Kellogg and Reid,

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Read June 6, 1930 before the American Association of Genito-Urinary Surgeons.

which is cognizant of the fact that renal conditions existing during pregnancy may simulate pre-eclampsia and eclampsia.

Pyelonephritis as the initial lesion of a trend resulting in progressive deterioration of the kidney has been emphasized by Weiss and Parker, by Longcope, and by others interested in the relation of chronic pyelonephritis to hypertension. Since the albuminuria and hypertension of toxemia of pregnancy may be associated with renal disease, it seems reasonable to investigate the incidence of toxemia following pyelonephritis in pregnancy. Mussey and Lovelady recently stated that pyelitis of pregnancy is not prone to cause pre-eclamptic toxemia or eclampsia. Although we may not agree with all of the conceptions and

TABLE I—CLASSIFICATION OF TOXEMIAS OF PREGNANCY—KELLOGG AND REID—1930

Group 1	
I	Hypertensive or arterial vascular disease
a	Benign
	Mild
	Severe—cardiorenal
b	Malignant
II	Renal disease
a	Glomerulonephritis
	Acute
	Chronic
	Mild
	Severe
b	Pyelonephritis
	Acute
	Chronic
c	Other forms of severe renal disease. Nephrosis, polycystic kidneys, and other congenital anomalies of the kidneys
Group 2	
I	Mild pre-eclampsia
II	Severe pre-eclampsia (Preconvulsive)
III	Eclampsia
Group C	
I	Unclassified (unknowns)
a	Those patients in whom a definite diagnosis can not be made to allow them to fall into Group A or B (i.e., glomerulonephritis suspected)
b	Many will fall into the above known groups post partum, but insuflcient data before or in the early months of pregnancy make it imperative to exclude them from statistical data except if autopsy findings ultimately allow them to be put in either Group A or B



Fig. 1. a, Primipara with left pyelonephritis in 01. b, Same patient in early pregnancy in 030. The urine

showed no infection. c, Same patient immediately post partum in 030. Late pregnancy changes not yet resolved.

conclusions presented by Peters, we acknowledge the importance of his success in focusing attention to the possible association of pyelonephritis to the toxemias of pregnancy. Of 320 cases with a diagnosis of toxemia studied by Peters, 41 or 13 per cent, had had pyelitis or pyelonephritis. The opinion was verified by autopsy in 11 of the 41 cases. Of 25 toxemia patients who came to autopsy during a 14 year period, Peters reported that in 11 or 44 per cent, pyelonephritis was found. However, closer scrutiny of the autopsies

data which were presented would lead us to believe that only 4 of the 11 cases, approximately 40 per cent, showed chronic pyelonephritic changes.

The important data supplied by Peters have been rather startling because of the relatively high incidence of pyelonephritis which he found in toxemia. We therefore recently decided to review a series of patients at the Boston Lying-In Hospital who we feel had pyelonephritis associated with at least one pregnancy and who



Fig. 2. a, left. Patient with pyelonephritis in sixth month of pregnancy. Moderate pregnancy changes in right ureter and kidney. b, Same patient 1 year later during another pregnancy. Urine was uninfected. There is less anatomical change than during the previous pregnancy.

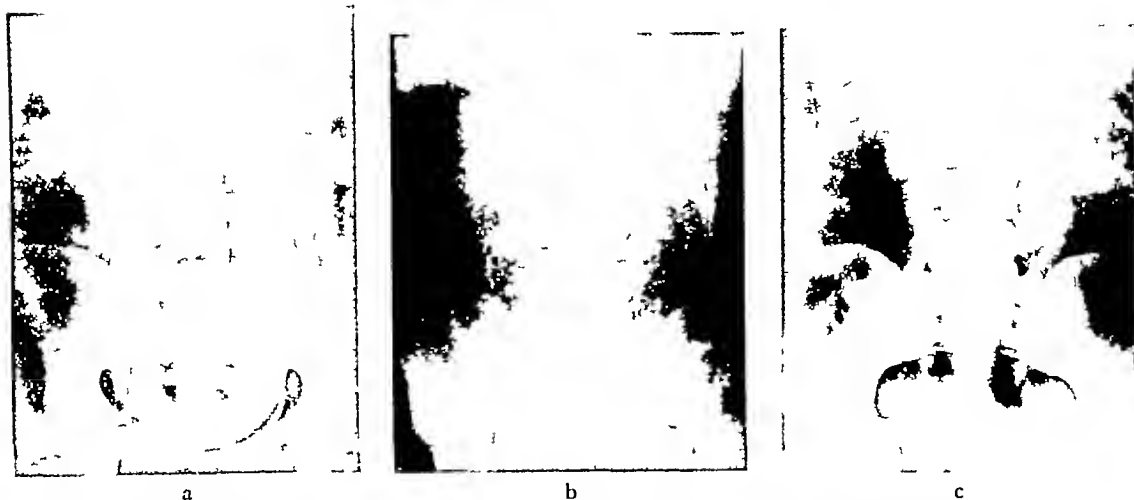


Fig 3 a, A quadrupara with pyelonephritis on the right side in 1930 during the eighth month of a pregnancy b, The same patient with pre-eclampsia during a preg-

nancy in 1933 c, The same patient postpartum There is evidence that a good anatomical recovery was made from the changes of pregnancy

returned during a later year in a pregnant state Such a review may give data as to how frequently toxemia follows the pyelonephritis associated with pregnancy

The data for this paper are based on the observations and records of 72 patients with pyelonephritis and pregnancy during the years 1930 to 1939 Only patients who had one or more pregnancies subsequent to the pregnancy with pyelonephritis were used Of the 72 patients, 42, or 58.3 per cent, were primipara, 30, or 41.7 per cent, were multipara Seventy had pyelonephritis dur-

ing pregnancy, 2 had acute pyelonephritis immediately postpartum while in hospital Forty-three, or approximately 60 per cent, were in a febrile phase while in hospital, leaving 29, or 40 per cent, in an afebrile, subacute stage at the time of observation

Further incidental clinical data of the patients forming our group indicated that pyelonephritis affected the right kidney in 48.5 per cent of the cases, the left kidney in 19.7 per cent of the cases, and in 31.8 per cent the inflammatory process was bilateral



Fig 4 a, Triparta with bilateral pyelonephritis in 1930 b, Same patient with toxic separation of placenta during a

later pregnancy c, Same patient at a later period, non-pregnant



Fig. 5 a, Tripara, in 1931, with pyelonephritis in the sixth month of pregnancy. The bony pelvis is abnormal. b Same patient in 1936, during her fifth pregnancy. Although there is bilateral hydronephrosis and hydroureter

the urine remained sterile. c, Same patient postpartum after her fifth pregnancy. It is evident that there has been good anatomical recovery of the kidneys and the ureters.

The records of these patients suggested a past history of pyelonephritis in 16.6 per cent, half of whom had had the disease with a previous pregnancy, the remaining half having had pyelonephritis before the onset of any pregnancy.

Our diagnoses were made by cystoscopic studies in 34 patients, clinical and laboratory findings in 38. Laboratory data revealed a bacillary type of urinary infection in 91.5 per cent, gram positive cocci in 5.1 per cent, bacilli and cocci in 3.6 per cent.

Renal function tests were not done as routine during the hospital admission for pyelonephritis, so that we do not have sufficient data from urea clearance studies and concentration tests to draw any conclusions. The nonprotein nitrogen in 40 cases was reported as 21 to 33 milligrams per 100 cubic centimeters of blood, and the blood ureic acid in 38 cases was recorded as 2.3 to 4.1 milligrams per 100 cubic centimeters of blood. Although we realize that blood chemistry does not detect slight diminution of renal function, it is evident that renal decompensation did not exist.

X-ray data were obtained in 55 patients—26 having had intravenous pyelography, the remaining 29 retrograde study. The dilatation of the ureters and pelvis (Fig. 1) and the lateral kinks were not extraordinary to anyone familiar with urological changes during pregnancy. The renal and ureteral dilatation in the subsequent pregnancies (Fig. 2) never exceeded that found with the first pyelonephritis, irrespective of whether the subsequent pregnancy was normal or compli-

cated by recurrent pyelonephritis or toxemia. In general, patients with toxemia appear to have less ureteral and pelvic distortion (Figs. 3 and 4) by intravenous pyelography than the normals. Extreme degrees of distortion and dilatation were observed frequently in patients with normal urine sediments and without clinical signs (Fig. 5) of pyelonephritis. The anatomical recovery following the physiological dilatation of pregnancy is impressive but is subject to continued distortion if abnormalities were present before pregnancy or if inflammatory changes in the pelvis or ureter go on to fibrosis.

Our primary interest in this study was not the findings in pyelonephritis, but rather how many later pregnancies were normal and how many were complicated by toxemia.

Of the 72 patients with pyelonephritis 47 or 65.28 per cent, had normal pregnancies at a later date. As a matter of fact, 5 of the 47 had further multiple normal pregnancies—a total of 67 normal pregnancies in 47 patients. The time interval between the pyelonephritis during pregnancy and the normal pregnancy varied between 1 and 9 years, an average interval of 3.62 years. Frequent blood pressure recordings were normal during the subsequent pregnancies in all 47 patients. Blood pressures during the normal later pregnancies were about the same as during pyelonephritic pregnancies in 34 patients. In 13 the readings averaged lower during normal pregnancy. Six of 47 patients had the slightest trace of albumin in a voided specimen just prior to term.

One normal pregnancy following a pyelonephritic pregnancy does not guarantee freedom from complications during a still later pregnancy. This fact is illustrated in 6 patients who developed pyelonephritis after having a normal intervening pregnancy, and 1 patient who developed toxemia of pregnancy after a normal intervening pregnancy.

Interest, of course, will be centered on those who had pyelonephritis during one or more pregnancies, and who in a later pregnancy developed toxemia. In our series of 72 patients who had pyelonephritis associated with pregnancy, and who later returned to hospital in a pregnant state, 9, or 12.5 per cent, developed toxemia. The hospital diagnosis as to the type of toxemia was pre-eclampsia in 8, eclampsia in 1, (toxic separation of the placenta with albuminuria in 1). The time interval between pyelonephritis in pregnancy and the toxemic pregnancy ranged between 1 and 9 years. The average interval was 3.45 years, essentially the same interval as mentioned above in discussion of the group who had subsequent normal pregnancies following pyelonephritis. Apparently the time interval is not important. Our data as to whether the urinary infection had cleared during the interval are incomplete. We are certain that of the 9 who developed toxemia, 2 patients had urines free of infection during the interval between pregnancies and 2 were known to remain infected. At the time of the pyelonephritis 4 were primiparas, 5 were multiparas. At the time of toxemia 3 were secundipara, 1 was a tripara, 1 was a quadripara, 3 were quintipara, and 1 was a decipara. The toxemia occurred in the first pregnancy following pyelonephritis of pregnancy in 7 of the 9. In 2 there was an intervening pregnancy with no indication of toxemia.

Renal function tests during the pregnancy with toxemia were not done as routine except for the nonprotein nitrogen, which was normal as one might expect. Table II shows the blood pressure readings in 9 patients with pyelonephritis who later developed toxemia. The toxemia was sufficiently severe in 5 of the 9 patients to warrant interruption of the pregnancy.

Because of the current interest in the relation between blood pressure and pyelonephritis, we present a meager amount of data which may be of interest. Of the 72 patients in our series there were 8, or 11.1 per cent, who during the pregnancy with pyelonephritis had, on one or more occasions, a blood pressure recorded of 140/90 or over. Four were in the ninth month of pregnancy, 2 were in the seventh month, 2 were in the sixth

TABLE II — BLOOD PRESSURE AND ALBUMIN

Case Number	Pyelonephritis			Toxemia		
	Year	Blood Pressure	Albumin	Year	Blood Pressure	Albumin
2	1935	118/74		1939	134/78	SPT ST
27	1937	110/86		1939	132/94	SPT
30	1936	150/110	1 ST	1939	150/84	LT
42	1930	108/80		1933	144/110	
47	1930	94/58		1931	170/114	LT
49	1930	108/80		1933	146/98	1 ST
64	1930	140/		1931	80/68	T
65	1930	10 /62		1933	(Hemorrhage) 105/65	SPT
71	1930	114/60		1939	170/100	

month. Three of the 8 had a past history of renal disease. The 8 patients just mentioned had 10 pregnancies following the one in which pyelonephritis and hypertension were observed. The time interval was 1 to 6 years, an average of 3.2 years. In the 10 pregnancies which followed, recurrent pyelonephritis developed in 5, but blood pressures remained below 130/85 at all examinations. Three normal pregnancies followed with all blood pressure readings 128/80 or below. Two developed toxemia with hypertension. In a follow-up of the 8 patients mentioned after an average interval of 3.7 years from the time of pyelonephritis with hypertension, all had blood pressure readings below 135/84. Only 1 patient had the slightest possible trace of albumin. Thus, in a small group of 8 patients with pyelonephritis and hypertension, toxemia developed at a later pregnancy in 25 per cent, which is double the incidence following pyelonephritis in general during pregnancy. However, our limited data fail to suggest any permanent elevation of blood pressure following pyelonephritis during a 3 year follow-up period.

On the basis of maternity hospital admissions, pyelonephritis has an incidence of 1 to 2 per cent (12). By the same standards, toxemia of pregnancy has an incidence of about 10 per cent (15). We have found that toxemia of pregnancy follows pyelonephritis associated with pregnancy in 12.5 per cent.

Not feeling competent to make accurate deductions from these simple figures we called upon Mr. Philip Rulon, who teaches statistics at Harvard University, for advice. His informal opinion was as follows:

A. The incidence of pyelonephritis in pregnancy is 1 to 2 per cent.



B The incidence of toxemia in pregnancy is 10 per cent.

The incidence of toxemia of pregnancy following pyelonephritis associated with previous pregnancy is 12.5 per cent.

Pyelonephritis is not a cause of toxemia of pregnancy.

The data for the proper deductions as to possible cause and effect should be tabulated in the manner here used, namely, to see how frequently disease B—toxemia—follows disease A, rather than the way in which Peters studied the problem, namely, how often disease A—pyelonephritis—occurs in disease B—toxemia. (According to Mr. Rulon there are too many variables in Peters's method of approach to warrant conclusions.) As for our data, which indicate an incidence of pyelonephritis in pregnancy of 1 to 2 per cent, an incidence of toxemia of approximately 10 per cent and toxemia following pyelonephritis in pregnancy is 12.5 per cent, Mr. Rulon states that if the same ratio held in 500 cases (we have only 72) we should be well justified in stating that

pyelonephritis is not a cause of toxemia of pregnancy.

#### BIBLIOGRAPHY

- BAIRD, D. and DE J. S. J. Path. & Bacteriol. 933, 57, 30.
- BELL, L. T. Am. J. Path. 912, 8.
3. FRIEDMAN, A. M. Hypertension and Nephritis 4th ed. Philadelphia: Lea & Febiger 1939.
4. IRVING, F. C. Canadian M. Ass. J. 930, 40, 17.
5. KELLOOG, F. S. and REED, D. F. To be published.
6. LONGCORE, W. T. Chronic bilateral pyelonephritis. Ann. Int. Med. 937, 40.
7. MCMURRY, R. D. and LOVELLADY, S. B. Am. J. Obst. & Gynec. 940, 30, 36.
8. PETERS, J. Yale J. Biol. & Med. 937, 9, 3.
9. Idem. J. Am. M. Ass. 938, 320.
- PETERS, J. et al. Am. J. Obst. & Gynec. 936, 3.
- PETERS, J. and ZIMMERMAN, H. T. Am. Am. Physiologists, 938, 5, 97.
- PRATHER, C. C. Urological complications during pregnancy. J. Indiana Stat. M. Ass. 937, 30, 17, 179.
3. WELSH, S. and PARSONS, F. Jr. Pyelonephritis. Medicine 930, 8, No. 3.
4. WILLIAMS, J. WENTWORTH. Obstetrics 4th ed. New York and London: D. Appleton & Co. 9.
5. Ibid. 7th ed., 936.

# MIXED INTRACRANIAL GLIOMAS

## The Diagnostic and Prognostic Significance of Adequate Histological Examination

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IT IS axiomatic that the accuracy of the diagnosis and prognosis of any neoplastic growth will vary directly with the amount and accuracy of the information available in regard to its histology and its location in the body. Such generalities are particularly applicable to the intracranial neoplasms. There are, to be sure, characteristics peculiar to this particular group of tumors which cause them to differ in detail although not in principle with these statements. For example, the usual intracranial neoplasm does not metastasize by way of the blood or lymph channels, but rather spreads locally either by expansion or by radial invasion. Such tumors, if irremovable, cause death, however, by virtue of the profound alterations produced in general, rather than local, central nervous system physiology. Thus, regardless of its histological character, any type of intracranial tumor can and will prove fatal when inaccessible and if properly placed in relation to the nervous structures around it. One phase of the brain tumor problem and of any attempt to estimate its end-results has to do, therefore, with a demonstration of the exact position of the tumor. This is well recognized and all of the modern advances in the therapy of intracranial tumors have depended, at the last analysis, upon the ability of the surgeon to make previously inaccessible areas accessible.

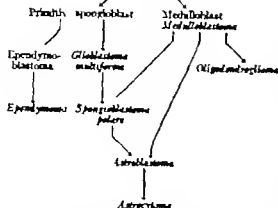
It is less well appreciated, however, that the histological make-up of the tumor is as important from a diagnostic and therefore prognostic viewpoint as its exact location. A circumscribed cerebellar medulloblastoma may be more accessible than the mural nodule in the upper wall of a large astrocytomatous cyst of the same region. Yet, apparently adequate removal of both will produce a lifetime cure in the latter and a life expectancy of not more than a year in the former. Such a difference in prognosis is demonstrable histologically at the time of operation. The importance of this operative histological study has been minimized by some neurosurgeons just as

the accuracy of so called pre-operative localizing signs has been overemphasized by some neurologists. At the last analysis, the final criteria of diagnosis and therefore removability must wait on exposure and adequate biopsy of the tumor either at operation or at autopsy.

These requirements apply in particular to the gliomas. A long step toward effective understanding of these tumors was taken with the publication of Bailey and Cushing's classification (Table I). Bailey further points out in a later publication that "*each type of glioma is a distinct entity with its own idiosyncrasies* which it is important to recognize. Any attempt to describe 'glioma' as an entity only leads to confusion. *In general the gliomas composed of cells resembling those of the early stages of histogenesis tend to develop more rapidly*." Of the groups that are commonly recognized the *medulloblastoma* and the *glioblastoma multiforme* are tumors that are closest to, and the *astrocytoma* the one that is furthest from the original medullary epithelium. In between these extremes lie, in approximate order of histological youth, the oligodendrogliomas, pinealomas, ependymomas, polar spongioblastomas, and astroblastomas.

It is obvious that tumors of adjacent cellular age may appear as histological mixtures. There have been expressions in the literature which bear on this point. Penfield has emphasized that the cells of any given glioma are originally derived from one primitive cell. With increasing age, differentiation becomes gradually more and more complete. Theoretically, therefore, it is possible to find cells representing varying phases of this differentiation in any one tumor. He reports that this idea is consistent with actual experience so that, for example, a tumor growing largely as an astrocytoma may contain spongioblasts and astroblasts. Globus (3) and Levine have each observed gliomas in which there was a mixture of cell types throughout the tumor. They are of the opinion that these cell types represent phases of glial development, and they have termed these tumors transitional cell gliomas. Carmichael has indicated

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TABLE I.  
Medullary epithelium

The relationships of the common cerebral gliomas. (Modified from Bailey and Cushing's classification. The choroidal, placoid and neuroblastic groups are omitted for purposes of simplification.)

that one cannot place every glioma into some one of Bailey and Cushing's groups because it is common to find a mixture of cell types within these tumors. Furthermore because gliomas frequently grow in part as polar spongio-glioblastoma and in other areas as spongio-glioblastoma (glioblastoma) multiforme he has suggested the name spongio-blastic glioma to include all tumors of the two types named. In tumors with greater cellular age Carmichael has found some areas in which the tumor was growing as astroblastoma and others in which there was the appearance of astrocytoma. He suggested the name of "astrocytic glioma" to include all tumors of the astrocytic and astro-blastic type whether occurring singly or together. Although those cases of Carmichael that showed mixture of types were usually confined to either the spongio-blastic or astrocytic groups, there were instances in which the tumor included elements from both. Others have also demonstrated a mixture of several types of glioma in isolated instances, among them being Globus and Strauss (4).

Gliomatous tumors composed of cells that are not developmentally adjacent should not be expected to occur under ordinary circumstances. Their frequent demonstration makes one suspect the orderly classification that thus places such cells at widely separated growth levels, and emphasizes what has already been recognized clinically—that is, that tumors that were histologically

benign have had lifecycles that were clinically malignant. Such a histological combination will be recognized materially influence the treatment accorded any given glioma. The recent demonstration of 9 such mixed gliomas is, on that account, worthy of attention. They occurred in the course of 4 years during which 143 verified intracranial tumors were seen on the neurosurgical service at the Boston City Hospital. Seventy-nine, 55 per cent, were gliomas and 28, 20 per cent, were meningiomas. All the other types formed a group of 35, 24 per cent. The present in the entire group of 6 per cent of mixed gliomas has a diagnostic and prognostic significance that cannot be overlooked. This is especially true when it is realized that these same 9 cases constituted 11 per cent of all the gliomas we encountered.

Four of the mixed tumors showed 3, and the others 2 cell elements. A part of every tumor was glioblastomatous, that is, the predominant cell was multiform, often a giant cell had frequent mitotic figures, and gave every evidence of being an immature actively growing tumor cell.

The balance of one of the tumors was classed as spongio-glioblastoma polare but this was the only one in which adjacent cell groups were co-existing alone.

CASE (N 8 3244 and 130-374) Male, aged 4 years. For one year previous to entrance this patient had been having frontal headaches. For 3 months previous to entrance he had had daily episodes of numbness in the right hand and forearm, right paralysis. On the day of entrance he had right sided convulsions, tonic, the last attack of consciousness and with some incoherence of the hands as well. On admission, he was irritable, inco-operative and disoriented. His general physical examination was negative. His blood pressure was 45/90 millimeters mercury. He had weakness of his right arm, right stereognosis and loss of position sense of the fingers of his right hand. He was right handed and there was some tenderness of the upper part of the right arm. Intracranial pressure of 30 millimeters after the cerebrospinal fluid was cleared. His hemoglobin, blood cell, total protein of 12 milligrams per cent and negative Wassermann and gold sol reactions. Roentgenogram showed marked displacement of the entire intracranial system to the right and down. The ventricular fluids contained 27 milligrams per cent of total protein on the right and left respectively. A left hemiparietal craniotomy, done and large infiltration of cortical and subcortical tumor as found. This was biopsied and diagnosed as glioblastoma multiforme. The dura was closed tightly and the bone flap as replaced. The patient died 4 days after operation.

A autopsy the brain weighed 500 grams. An area of operation interference, centimeter in diameter as present in the region of the left superior parietal gyrus. In the left parietal region serial sections showed all areas described area 1 centimeter in diameter that as closely as the white matter but which infiltrated the gray matter slightly as cell. The tissue was yellow gray with brown periphery and softer central portions.

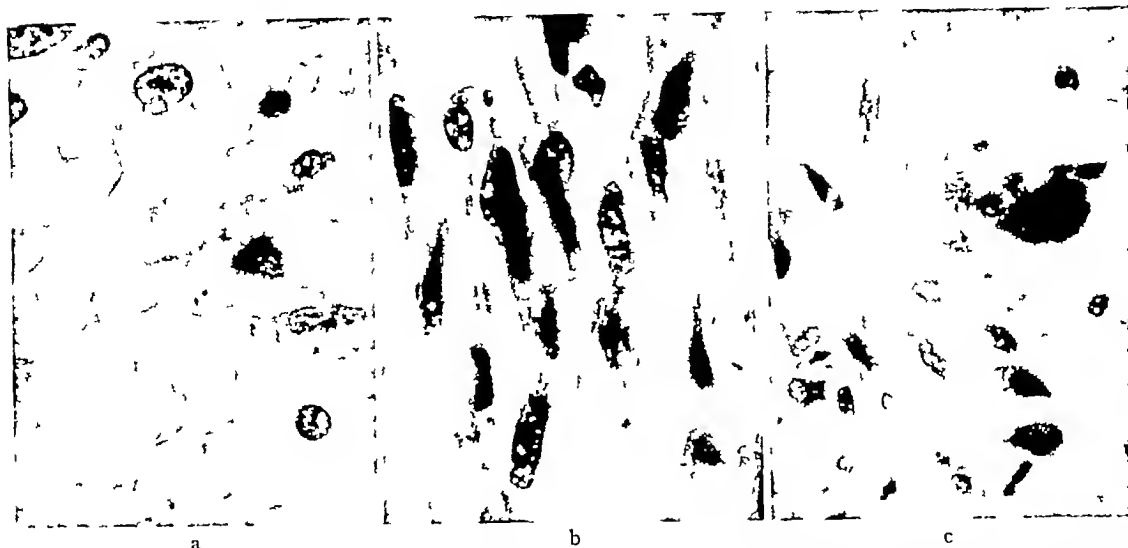


Fig 1 a, Astrocytoma showing numerous neuroglial fibrils Mallory's phosphotungstic acid hematoxylin stain  $\times 745$  b, Fusiform cells arranged in parallel rows No intercellular fibrils This area is typical of a polar spongi-

oblastoma Mallory's phosphotungstic acid hematoxylin stain  $\times 745$  c, Glioblastoma multiforme showing two mitoses and a tumor giant cell Mallory's phosphotungstic acid hematoxylin stain  $\times 225$

Microscopically this tumor showed two fundamental pictures. The major part was growing as a polar spongioblastoma. There were spindle cells with long, fairly well stained cytoplasmic processes, an occasional mitosis, and no intercellular fibrils. This picture was similar to that seen in Figure 1b of Case 2. In a smaller number of fields the tumor failed to show any regularity and tumor giant cells similar to that in Figure 2c of Case 4 were found. We consider these latter areas characteristic of glioblastoma multiforme.

Four other tumors that contained both glioblastomatous and spongioblastomatous tissue had in one case an additional undifferentiated part that resembled medulloblastomatous tissue and in the 3 other cases additional astrocytomatous (twice) and oligodendrogliomatous sections as well.

Case 2 (Nerve, A 36 450) Female, aged 56 years. For 1 month previous to entrance she had complained of increasing weakness and staggering gait, falling to the left, transient diplopia, headache and drowsiness with difficulty in thinking. For a few days before admission, she had been vomiting and had felt weak. She lost 10 to 12 pounds in this month. There had been no injuries or illnesses in the past. General physical examination was negative except for pallor and signs of recent weight loss. She was drowsy and unco-operative. She showed a left hemiparesis including the lower facial region. The deep reflexes were increased on the left. There were bilateral Babinski, Oppenheim, and Gordon signs. There were high choked discs and she was unable to count fingers with the left eye at 3 feet. Her blood pressure was 90/60 millimeters mercury. She had a slight anemia and a positive blood Hinton. Lumbar punc-

ture showed an intracranial pressure of 470 millimeters water with normal dynamics. The cerebrospinal fluid had 51 white blood cells, 10 per cent of which were polymorphonuclears, a total protein of 78 milligrams per cent, and a doubtfully positive Kahn test. Other specimens showed cells as high as 1,300, from 25 to 100 per cent polymorphonuclears and total proteins from 130 to 750 milligrams per cent. She died suddenly and untreated 8 days after admission.

At autopsy the brain weighed 1,270 grams. There was a moderate cerebellar pressure cone with widening and flattening of the cerebral convolutions. In the right cerebral hemisphere, there was a huge tumor mass extending posteriorly from the anterior tip of the right frontal lobe to a level 5 centimeters anterior to the tip of the occipital lobe. Laterally the tumor extended to the surface of the cerebral substance and medially to the lateral border of the right thalamus. The tumor tissue was soft yellowish white and possessed a purplish brown border.

Microscopically some areas of the tumor showed well differentiated cells with prominent intercellular fibrils staining purple with the phosphotungstic acidhematoxylin stain. These areas may be considered characteristic of astrocytoma (Fig 1a). Other areas showed definite spindle-shaped cells whose cytoplasm stained fairly well. There were no intercellular fibrils. In these areas the tumor resembled a polar spongioblastoma (Fig 1b). In other regions were poorly differentiated cells with mitotic figures and tumor giant cells characteristic of glioblastoma multiforme (Fig 1c).

Case 3 (N S 3350, S 30 2790) Male aged 64 years. One year and 10 months before admission this patient complained of substernal burning of 1 month's duration. A diagnosis of cardiospasm was made in another hospital.

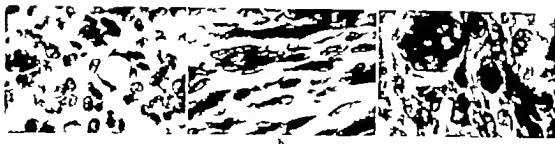


Fig. 1. a, Poorly differentiated tumor with rather uniform cellularity and absent giant cells—suggests meningeal loblastoma. Mallory's phosphotungstic acid hematoxylin stain. X500. b, Characteristic pattern of polar spongi-

oblastoma. Mallory's phosphotungstic acid hematoxylin stain. X500. Large immature cells and one tumor giant cell typical of glioblastoma multiforme. Mallory's phosphotungstic acid hematoxylin stain. X500.

This diagnosis was changed 3 months later to arteriolethrombotic heart disease with coronary insufficiency and angina pectoris. He was given  $\frac{1}{2}$  grain of benzal 4 times daily and was free of symptoms 1 month later. Vasodilators at that time were not so common. His chief complaint was of a circumscribed area over the right temple. He was seen at the Boston City Hospital for the first time 6 months before his final admission. He complained of bilateral supra-orbital pain, numbness over the scalp, and sensation of peculiar odors. Examination showed papilledema of 3 disc diameters but no localizing signs. A diagnosis of brain tumor—suspect of metastatic origin—was made. A month later his memory began to fail and he developed personality changes. He refused to permit adequate investigation at that time. On his final admission he was in deep coma. There was no history of injury or disease except as noted. On physical examination he showed a slightly enlarged heart, generally depressed tendon reflexes, left homonymous, and choking of 4 disc diameters. He responded only to painful stimuli. His blood pressure was not recorded. Lumbar puncture showed an intracranial pressure of 40 millimeters of water. The cerebrospinal fluid was clear and colorless. Without cells and with total protein of 3 milligrams per cent. A cerebrogram as done the day after admission. It showed displacement of the anterior horns and the third ventricle to the left with dilatation on the left. The right ventricle was not entered with the needle, being overlaid by a cyst which then was visible as a separate structure in the right temporo-occipital region. The cyst fluid had total protein of 3.50 milligrams per cent and the left ventricular fluid one of 47 milligrams per cent. A low right parieto-occipital craniotomy was performed. This revealed an extensive infiltrating tumor which lay astride the Sylvian fissure. On section, the tumor was found to be tough and had the appearance of meningioma. A biopsy was done. The diagnosis from this tissue as reported as malignant metastatic tumor, probably carcinoma, and with many mitoses. No further attempt at removal was made. The dura was closed tightly and the bone flap replaced. The patient did not regain consciousness and died 24 hours later. No autopsy was permitted.

Later and more detailed study of the biopsied tissue changed the original diagnosis. Microscopically the tumor showed large areas in which the cells were well differentiated. The cytoplasm stained poorly however and the nuclei varied in shape from ovoid to spherical. Numerous intercellular neurofibrillar fibers were present. In such

areas the tumor was considered to be growing as an astrocytoma, the tissue being similar to that shown in Figure 7a of Case 9. In other areas the picture was that of a polar spongioblastoma. The tumor cells were fusiform and had cytoplasm that stained fairly well. No intercellular fibrils were present. The appearance here was similar to that shown in Figure 1b, Case 2. In still other fields the cells were poorly differentiated, with tumor giant cells and moderate numbers of mitoses. We consider this appearance characteristic of glioblastoma multiforme shown in Figure 5c, Case 7.

CASE 4 (N. S. 3035, A 38493). Male, aged 64 years. Three months before entrance this patient began to have severe throbbing, greenish headaches, shortly followed by repeated grand mal type of convulsive seizures. He had had no such during this period. The cells before admission his left side became weak. There was no other significant family or past history. On admission he was lethargic and somnolent. His an evident memory defect. Physical examination as noncontributory except for the fact that he kept his head rotated to the right and that he had an enlarged boggy prostate. His blood pressure was 140/90 millimeters of mercury. He showed left homonymous and homonymous hemianopia. His position Babinski, Gordon and Oppenheim signs, the last being present on his right as well. The right disc was choked and the left could not be seen on account of lenticular opacities. There was negative blood Hinton. Lumbar puncture showed an intracranial pressure of 350 millimeters of water. His normal dynamics. The cerebrospinal fluid was clear colorless, without cells and had total protein of 0.3 milligrams per cent and gold sol of 12 units. Six days after admission, a cerebrogram was done. It showed displacement of the ventricles to the left and in addition shadow which looked like a separate lesion projecting into the lateral ventricle on the left. Fluid with total protein of 6.900 milligrams per cent was obtained from cyst on the right at this time. The left ventricular fluid had 7 milligrams per cent of protein. A right posterior parietal craniotomy was done 10 days later. A soft subcortical scular tumor was found in the temporo-parietal region. The biopsy tissue as reported as being identified as an astrocytoma. Excision as out of the question, on account of the tumor's size, so after providing small decompression, the rest of the dura was closed and the bone flap replaced. The patient died 48 hours later without regaining consciousness.

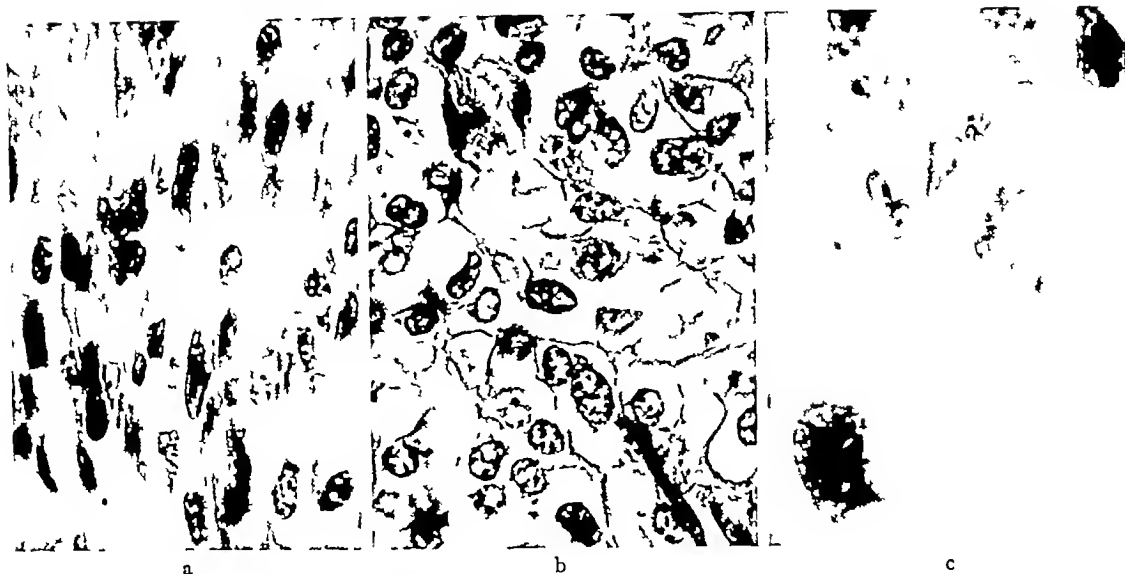


Fig 3 a Typical arrangement of cells of a polar spongioblastoma Phloxine methylene blue stain  $\times 745$  b, Rather uniform cellularity with prominent cell margins and little intercellular substance Strongly suggestive of

oligodendroglioma Phloxine methylene blue stain  $\times 745$  c, Tumor giant cell and undifferentiated cells characteristic of glioblastoma multiforme Phloxine methylene blue stain  $\times 745$

At autopsy the brain showed diffuse widening and flattening of the convolutions. In the right occipital pole there was a well circumscribed firm tumor measuring 4.0 centimeters in diameter. The center of the mass showed numerous cyst like spaces measuring up to 2.0 millimeters in diameter and containing a light greenish yellow coagulum. In addition, in the superior portion of the right parietal lobe, there was a moderately firm, well circumscribed tumor measuring 1.3 centimeters in diameter.

Sections taken from the two tumors exhibited three types of glioma. In some fields the cells were fusiform with polar cytoplasmic processes. There were no intercellular fibrils. We may consider these areas as exhibiting the characteristics of a polar spongioblastoma (Fig 2b). Another area exhibited poorly differentiated tumor cells whose cytoplasm stained very faintly. The nuclei were vesicular with prominent nucleoli. The nuclear shape varied from round to oval. There were no giant cells. Although for the greater part there was no characteristic arrangement, there was a suggestion of pseudo-rosette formation in a few instances. Intercellular fibrils were absent. We may consider this part of the tumor as a medulloblastoma (Fig 2a). Associated with the regions appearing as polar spongioblastoma there were some areas showing larger cells than in either of the above. These cells showed poor differentiation and in some instances true tumor giant cells were encountered. We may consider these latter fields as exhibiting the criteria of glioblastoma multiforme (Fig 2c).

CASE 5 (N S 3273, A-30-444) Male, aged 44 years. This patient was known to have been a chronic alcoholic for a number of years, and he was believed to have had weakness of his legs for 5 years but more detailed information was lacking. He may have had a head injury 9 months previous to admission. Three months before admission, he was taken to another hospital during an alcoholic spree. While there, he developed bronchopneumonia and in the course of his stay was found to have had "marked generalized hyperreflexia, dysmetria, ataxia, sluggish pupils and bilateral choked discs." A lumbar puncture at that time showed an intracranial pressure of 500 milligrams of water. The cerebrospinal fluid was found to have had a total protein of 80 milligrams per cent. On this last admission, he was disoriented and ataxic and had noticeable weakness of his legs. Physical examination demonstrated atrophy of the muscles of his left arm, both shoulders, and both legs. His blood pressure was not recorded. He had bilateral high choked discs, nystagmus, dysmetria, and ataxia. He staggered and fell toward the left. There was marked weakness of the left hand. He had hyperactive tendon jerks, bilateral ankle clonus, and Babinski signs. The Weber test was lateralized to the right. Two days after admission, a ventricular estimation demonstrated a marked bilateral hydrocephalus with 10 and 9 milligrams per cent of protein in the right and left ventricular fluids, respectively. No air was put in the ventricles. Immediately following this procedure, a suboccipital craniotomy was started. It had to be abandoned after removal of the bone on account of excessive bleeding. The patient died without regaining consciousness about 8 hours later.

At autopsy, in addition to an intraventricular hemorrhage and bilateral bronchopneumonia, a tumor of the cerebellum and brain stem was found. The brain weighed 1,350 grams. A moderate cerebellar pressure cone was found. There was a moderately firm tumor lying beneath the pia arachnoid and involving the right cerebellar tonsil, brachium pontis, and the restiform body. The neoplasm measured 4 by 2 by

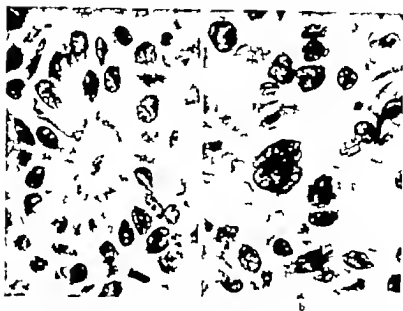


Fig. 4. a. Gland like arrangement of cells. It is biphasic. This is characteristic of an ependymoma. Mallory's phosphotungstic acid hematoxylin stain.  $\times 760$ . b. Poorly differentiated cells. It is tumor giant cell. This is indicative of glioblastoma multiforme. Mallory's phosphotungstic acid hematoxylin stain.  $\times 760$ .

centimeters and on cut section revealed nodular surface which for the greater part showed light yellowish gray color in which are smaller light brown areas measuring up to 5 centimeter in diameter. There is moderate distention of the lateral ventricles.

Microscopically the tumor exhibited considerable variation in appearance from field to field. In some areas the tumor had the appearance of a polar spongioblastoma, the cells being of moderate size and spindle shaped (Fig. 3a). Inter cellular fibrils were absent. In still other fields there were sheets of tumor cells with prominent cell margins which gave them the appearance of an oligodendroglioma (Fig. 3b). In other areas there was the haphazard cellular arrangement with tumor giant cells that is indicative of glioblastoma multiforme (Fig. 3c).

Four other tumors had in addition to the glioblastomatous, ependymomatous theme (twice) and astroblastomatous or astrocytomatous sections once each.

CASE 6 (N. S. 586, S-30-3094) Male, aged 3. This patient as ill until January, 1937. At that time he suddenly developed diplopia. Four months later he had severe frontal headache accompanied by nausea and vomiting. Four months later he as first admitted to the hospital. He had had no previous history of injury or other significant illness. Glasses had relieved his headaches before admission but transitory attacks of diplopia persisted. Physical examination revealed an ill developed and poorly labeled boy of 3 years. His genitalia are small and the

right testicle as undescended. His as co-operate and oriented conscious and rational. There is enlargement of the left external rectus muscle and of the left side of the face of central type. The discs are markedly choked and exoptal as present. There is right homonymous hemianopsia. His tongue deviated to the right. The tendon reflexes are all markedly depressed or absent. There are bilateral Babinski and Chaddock signs. His blood pressure as not recorded. His pulse, temperature and respirations are all normal. There is noticeable tenderness of both hands. A lumbar puncture showed an intracranial pressure of 350 milligrams of water. The cerebrospinal fluid as clear and colorless. Its total protein of 45 milligrams per cent. The rest of the laboratory tests are normal. A diagnosis as made of left cerebral tumor and left posterior parietal craniotomy as performed. A large cyst as tapped in the lower parietal area. This as opened and drained after which large bluish red, vascular and cellular tumor as found on its medial side. A piece as removed and examined microscopically. As result, it as reported to be an ependymoma. Further exploration demonstrated that the tumor had invaded the skull and partly filled the cavity of the lateral ventricle. It as very vascular and so as left intact except for the biopsy. A decompression as provided, and the bone flap replaced. After stormy convalescence he as discharged to his home. At that time he as aphasic, had bilateral motor weakness and urinary incontinence. The choking had disappeared and the vocal folds, especially that on the left, are noticeably improved.

For year and one half he continued to improve and became practically normally active. At the end of that time he had his first convulsion attack. Eight months later having completed at home the work done in public schools by boy of his age, he again had diplopia and early choking of his discs was again discerned for the first time.

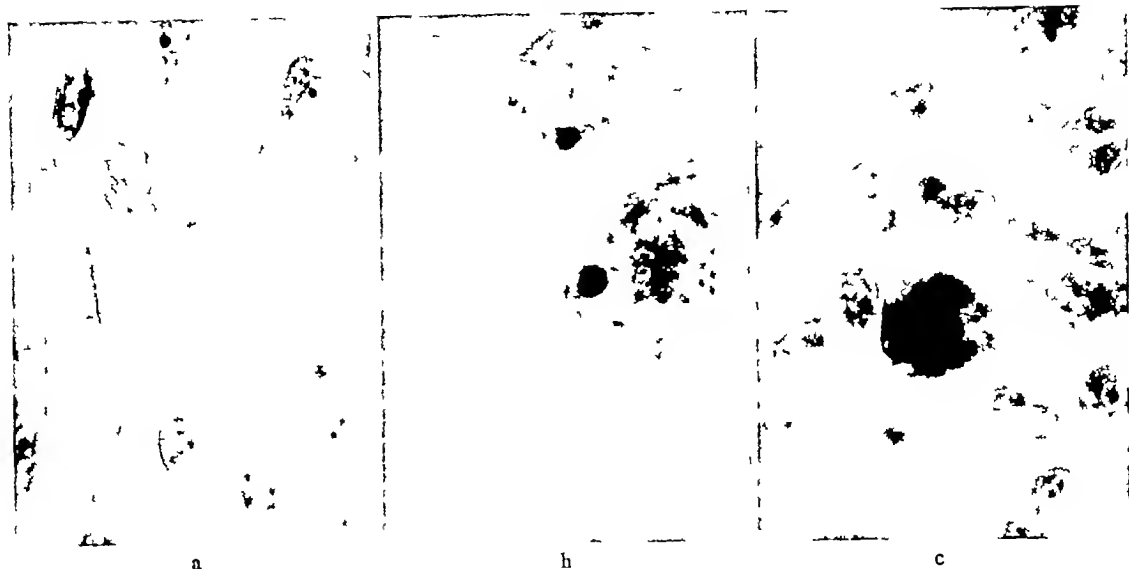


Fig 5 a, Large spindle cells arranged in a palisade formation with coarse intercellular fibrils. Suggestive of ependymoma. Mallory's phosphotungstic acid hematoxylin stain  $\times 745$  b, Numerous intraprotoplasmic and heteroplastic granules. These cells establish the diagnosis of

ependymoma. Mallory's phosphotungstic acid hematoxylin stain  $\times 1490$  c, Haphazard cellular arrangement with tumor giant cells. This is characteristic of glioblastoma multiforme. Mallory's phosphotungstic acid hematoxylin stain  $\times 745$

He was given x ray therapy and 2 months later was improved. One month after completion of a series of 20 treatments, he was readmitted to the hospital because of increasing drowsiness to coma for the previous 24 hours. This was 2 years and 9 months after the onset of his symptoms and 2 years and 3 months after his operation. He had all the signs of increased intracranial pressure. The right ventricle and the cyst on the left were emptied through the old trephine holes as an emergency measure and 10 days later the old craniotomy wound was reopened. A radical resection of the tumor that now filled the ventricle and invaded large areas of the parietal and temporal lobes was done. Many cysts were encountered, much tissue was soft enough to suck out, and much was very firm and fibrous and had to be removed by sharp dissection. He had a stormy convalescence with severe headaches, a right hemiparesis, and profound aphasia. During his hospital stay he was given another series of x ray treatments and eventually was sent home 2 months after admission able to speak normally, without choked discs, and active all day with the aid of a cane and an orthopedic brace to control his foot drop. He still had a right homonymous hemianopsia. He has continued to improve during the succeeding 6 months to date.

A complete histological study was carried out on the tissue that was removed at the last operation. It was composed, in gross, of many pieces of friable gray tissue, the aggregate mass measuring 3.0 cm in diameter.

Microscopically, some regions of the tumor showed fairly well differentiated cells. In some instances these were columnar in shape and assumed gland-like formation. The cytoplasm beneath the margin of the gland-like spaces contained moderate numbers of diaphanoplastin granules (Fig 4a). These areas were considered charac-

teristic of ependymoma. In other areas the tumor appeared as a glioblastoma multiforme with lack of cell uniformity and the presence of multinucleated tumor giant cells (Fig 4b).

CASE 7 (N S 2950, S 38 1696). Male, aged 53 years. This patient had been entirely well up to 2 weeks before his admission. At that time he had "bumped his head" without unconsciousness or other immediate symptoms. Frontal headaches developed for which he consulted his local doctor and was told that he had "sinusitis." For the week previous to admission he was unable to read and was "out of his mind." On admission he was completely aphasic, disoriented, and confused but co-operative. Physical examination showed moderate arteriosclerosis, bilateral high choked discs, right homonymous hemianopsia with sparing of the maculae, dilated fixed pupils, alexia, and partial sensory and motor aphasia. There was no astereognosis. The patient was right handed. The tendon reflexes were within normal limits, and there were no abnormal reflexes. He had a high intracranial pressure (230 mm water) with cerebrospinal fluid that was clear, colorless, without cells, and with a total protein of 70 milligrams per cent. Serological tests were all negative. His blood pressure was 128/70 millimeters of mercury. Two weeks after admission a left temporoparietal craniotomy was performed. A large soft infiltrating cystic tumor of the temporal lobe was widely removed. Microscopic diagnosis at the time of the operation was glioblastoma multiforme. A decompression was provided, and the bone flap was replaced. He made a satisfactory convalescence and returned home 2 weeks after the operation with a normal intracranial pressure but with all his other symptoms and signs just as they were before operation. During the succeeding 6 months at home he gradually went downhill and after a week of unconsciousness, died 8 months after he had noticed his first symptom. There was no autopsy.





Fig. 6. a. Pyramidal shaped cells with sucker feet attached to the wall of blood vessel. This is characteristic of astroblastoma. Mallory's phosphotungstic acid hematoxylin stain.  $\times 555$ . b. Haphazard cellular arrangement with tumor giant cell. This is characteristic of glioblastoma multiforme. Mallory's phosphotungstic acid hematoxylin stain.  $\times 555$ .

A complete histological examination was carried out on the tissue removed at operation. This was in the form of several fragments of firm to gritty gray-white tissue, the largest measuring 1.5 centimeters in diameter, the smallest 0.4 centimeters.

In some microscopic fields the tumor cells were elongated, fleshy and arranged in palisade formation. There were coarse intercellular fibrils (Fig. 5a). Some cells exhibited numerous blepharoplast granules in their cytoplasm thus establishing the diagnosis of ependymoma (Fig. 5b). In other fields there was no orderly cellular arrangement nor any intercellular fibrils. Mitotic figures were numerous and tumor giant cells were present in moderate numbers. We classify the tumor in these fields as glioblastoma multiforme (Fig. 5c).

**CASE 8** (N. S. 3053, 5-35-700). Female, aged 39 years. For 5 months before admission, this patient had been having left frontal headaches and increasing somnolence. At the time she first noted these symptoms, she was 8 months pregnant. Two months before admission, she fell. Following that she began to act abnormally, talked out of one side of her mouth, and developed weakness of her left hand. Having always been left-handed she now began to use her right hand almost exclusively. Her left leg, face, and shoulder progressively became weaker until she had complete left hemiplegia. For 1 month before admission, she had moderate aphasia and for 1 week she had been vomiting and complained of loss of sight in her left eye. On admission, she was stuporous and restless. She had had no significant previous illnesses or injuries. Physical examination demonstrated that she was 8 months pregnant, had left hemiplegia, arteriosclerosis on the left and aphasia. Her blood pressure was not recorded. At lumbar puncture she was shown to have an intracranial pressure of 30 millimeters of air. The cerebrospinal fluid was clear, colorless, without cells and had total protein of 86 milligrams per cent. Blood and cerebrospinal fluid Wassermann and Hinton test are negative. She showed trace of sugar but no albumin in its urine examination. She had secondary aneurysm. Two weeks after admission she was delivered of a baby by cesarean section. The baby, however, died in a few days of hemorrhagic disease of the newborn. The mother convalesced as usual.

Three weeks after the cesarean section, craniogram showed the right lateral ventricle to be compressed, the both ventricles displaced to the left and a large cyst in the middle region of the right cerebral hemisphere. The left ventricular fluid had total protein of 100 milligrams per cent and the cyst one of 4,650 milligrams per cent. The following day, right posterior parietotemporal craniotomy was done. The subcortical cyst was opened just above the supramarginal gyrus, and tumor tissue, as demonstrated posterior and superior to it. Microscopic examination of biopsied specimen of this tissue, as reported as showing rapidly growing astrocytoma. This cyst, all as destroyed and small amount of tumor removed. It proved to be impossible to replace the bone flap, so it was sacrificed, the dura being closed except on the posterior inferior margin. After stormy convalescence complicated by cerebrospinal fluid fistula through the scalp wound, she got up and about the third day and as allowed to return home 3 months after admission. There was considerable bulging of the decompressed area.

For 3 months she was comfortable and moderately active about her home. She had no symptoms and was bothered only by the increasing size of the decompression. At this time she began to be disabled by an increasing headache and hemianopsia. Her blood pressure was 140/84 millimeters of mercury. She was readmitted for possible re-operation. This was attempted but had to be abandoned on account of cerebral bleeding. The wound failed to heal, fungus developed, she became rather irrational and confused, and eventually died 4 months later, 1 year and 3 months after her first symptoms and 1 year and 3 months after her first operation. There was no autopsy.

The tissue removed at the first operation was subjected to a later more detailed study. It was an egg-shaped mass measuring 5.5 by 3 by 2.5 centimeters. The tissue cut with moderate resistance and the cut surface presented alternating areas of white, lemon yellow and black.

Microscopically the tumor was largely composed of cells whose nuclei were fairly vesicular and cytoplasm indistinct. Intercellular fibrils were absent. About blood vessels the tumor cells appeared fusiform with fairly well defined sucker feet attached to the endothelium. This part of the

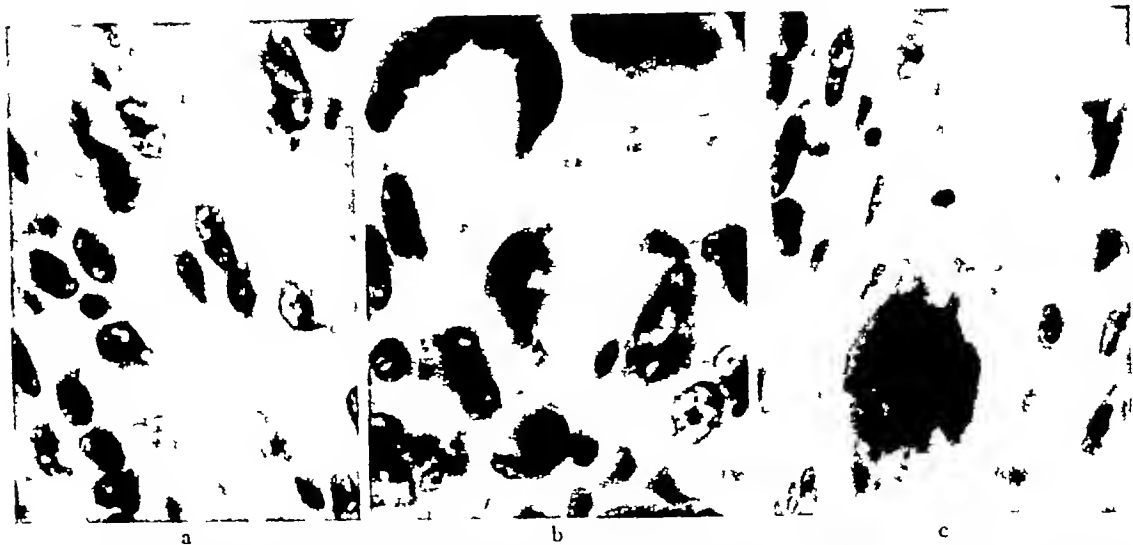


Fig 7 a, Well differentiated cells with numerous neuroglial fibrils. This is characteristic of an astrocytoma. Hematoxylin and eosin stain  $\times 745$ . b, Huge giant cells somewhat resembling foreign body giant cells. These

probably represent multinucleated astrocytes. Hematoxylin and eosin stain  $\times 745$ . c, Large tumor giant cell establishing the diagnosis of glioblastoma multiforme. Hematoxylin and eosin stain  $\times 745$ .

tumor was considered to be an astroblastoma (Fig 6a). In other scattered fields mitotic figures were fairly numerous and occasional tumor giant cells were found. This tissue we consider typical of glioblastoma multiforme (Fig 6b).

CASE 9 (Private, S-38 1967). Male, aged 67 years. This patient had been well and active until 9 months before admission. At that time he was injured in an automobile accident having been struck on the right temple. He was unconscious for a short period. He remained active in business for 7 months after although it was noted that during that time he became more and more irritable and forgetful and was easily depressed and fatigued. At this time he first complained of "stiffness" of the left hand and arm to which a sense of numbness and awkwardness was added after he had been curling on one occasion. Ten days before admission he had a convulsive seizure involving his left hand, arm and face without loss of consciousness. This was repeated at intervals until admission. The attacks were preceded by paresthesias in the same distribution. Physical examination showed normal eye grounds, obesity, arteriosclerosis and a flaccid paralysis of the left hand and arm with absent tendon reflexes. There were increased knee and ankle jerks with the left greater than the right, slight bilateral ankle clonus and no abnormal reflexes. There was a left hyposthesia. His heart was enlarged to the left and there were some moist rales at the bases of his lungs. His blood pressure was 180/100 millimeters of mercury. At lumbar puncture an intracranial pressure of 100 millimeters of water was demonstrated. The cerebrospinal fluid was clear, colorless, had 3 lymphocytes and a total protein of 47 milligrams per cent. Roentgenograms of the skull showed the pineal gland in normal position. A diagnosis of cerebral subdural hematoma suspect was made and 4 weeks after admission a right craniotomical exploratory trephination was done. It was noted that the temporal lobe was softer to palpation than the rest of the brain and after removal of about 40 centimeters of fluid

that was thought to be but could not be proved to be subdural fluid the brain fell away about  $\frac{3}{4}$  inch from the under surface of the dura. The dura was left open and the wound was closed about a drain which was removed 24 hours later. The fluid collected at operation proved to have a total protein of 45 milligrams per cent. The operation made no change in his symptoms or signs. He gradually grew weaker and more confused, had an occasional generalized convulsive seizure and died 5 weeks after operation after a short period of unconsciousness.

At autopsy, the brain showed an extensively infiltrating tumor involving the right frontal and parietal lobes.

The microscopic sections showed considerable variation in appearance with the tumor growing fundamentally as an astrocytoma and as a glioblastoma multiforme. In some areas the cells were well differentiated although their cytoplasm stained poorly if at all, and there was an abundance of intercellular fibrillar substance (Fig 7a). A number of fields showed numerous giant cells which appeared to be of two types, one of which showed considerable cytoplasm with a rim of well differentiated and relatively small nuclei. These cells had some similarity to foreign body giant cells as seen outside the central nervous system and probably represented the giant astrocytes described by Penfield (Fig 7b). These findings were considered typical of an astrocytoma. Other giant cells showed a relatively small amount of cytoplasm and large irregular nuclei, a picture characteristic of tumor giant cells (Fig 7c). These cells were associated with a moderate number of mitoses. This picture was consistent with the diagnosis of glioblastoma multiforme.

If Bailey and Cushing's theory of progressive cellular age in the development of gliomas is correct, it will be evident that the combinations here described not only bring together in one mass cells at opposite ends of a single family tree, but also cells from two entirely discreet families. No explanation is offered to account for this bizarre cellular grouping. It is merely recorded in the hope and expectation that it, together with other similar observations will eventually help to clarify the glioma problem.

In the meantime and from the clinical point of view the malignancy of glioblastomas, the benignancy of astrocytomas, and the appropriate varying degrees of malignancy of the intervening tumors must be accepted as the present foundation on which to build surgical therapy. Even this statement must be regarded as only temporary, however. Scherer, in an article entitled "The Forms of Growth in Gliomas and Their Practical Significance" presents conflicting evidence which if confirmed, may be taken as demonstrating that a considerable percentage of glioblastomas are therapeutically favorable and that all astrocytomas are invariably therapeutically unfavorable tumors. Lacking such confirmation, it is better for the present to adhere to the more orthodox and older beliefs. From this point of view the potential inaccuracy of the biopsy diagnosis made at the time of the operation in this series is striking. There was a failure to identify histologically at this time the presence of the most unfavorable type of tumor cell in 4 of 6 cases, and in only 1 case was the co-existence of the more benign cells accurately recognized. In 2 other instances, the presence of a tumor was not even suspected even though one patient was explored in the attempt to make a diagnosis. In the remaining patient, a pre-operative diagnosis of neoplasm was made but the tumor could not be exposed on account of the man's condition.

Little help in detecting the type of tumor was had from the history and examination. Of the two the history was probably of greatest significance. The one cerebellar tumor caused recognizable symptoms for 5 years before the patient consulted physician about them. However the patient suffered from chronic alcoholism for which he was hospitalized several times. At his final admission he was in coma and the history was obtainable only from friends and previous hospital records. In no other instance did this period exceed 6 months and in one the patient himself repeatedly stated before and after the diagnosis had been made that his symptoms preceded his hospitalization by only 2 weeks. In 1 case hos-

pitalization was brought about because of an acute exacerbation of previously negligible symptoms by pregnancy. A living 8 months baby was delivered by cesarean section but it died of hemorrhagic disease in a few days. One month later subtotal resection of mother's tumor was done.

The location of the cerebral tumors was also without diagnostic or prognostic significance.

The postoperative survival period was of no significance. It was conditioned by such uncontrollable factors as previous alcoholism, inadequate food, pregnancy, syphilis, age, misleading history, the presence of a cyst in the tumor and so forth. The only patient with a significant survival period is one that had a combined glioblastoma and ependymoma which was partly intraventricular. He is still living at the age of 16, 3 years after his first operation. One of the 2 correctly diagnosed cases, as far as the glioblastomatous part went, lived 6 months and the other 9 days after operation. Only a small biopsy was done in the latter. One patient with a tumor that was partly glioblastomatous and partly astroblastomatous lived 14 months and another with a tumor that was partly astrocytomatous lived 5 weeks. The former had a subtotal resection and removal of the bone flap at her first operation followed by repeated tapplings of a cyst and 2 secondary operations. The latter did not even have his tumor exposed. Four tumors were cystic in part, the rest being completely solid. Two cases died because of peripheral circulatory failure 48 hours and 14 months after the first operation. One died because of a ventricular hemorrhage 12 hours after operation, in one the cause of death was not determined and the remaining patients died of massive cerebral edema with a cerebellar cone from a few hours to 9 days after operation.

Failure to make a correct histological diagnosis of the tumor at the time of operation was due to one chief factor. In this connection, it is obvious that those cases in which the tumor was not seen because of poor or inadequate operative exposure can be eliminated. With these eliminated there are 31 tumors which were classified from material removed at operation only and 3 in which postmortem studies were made in addition. Regardless of anything else the important datum to obtain at the earliest possible moment about any intracranial tumor is whether or not it is wholly or partly made up of malignant glioblastomatous or medulloblastomatous tissue. As a corollary to this, care must be taken, of course not to confuse the giant astrocytes described by Penfield as occurring in astrocytomas (Fig. 7b) with the true tumor giant

cells that characterize the glioblastomas. Thus, the ultimate measure of success that attends any attempt at classifying histologically a given tumor rests on the ability of the pathologist to recognize, while the operative field is exposed, the presence of either one of these 2 cell groups regardless of whether or not any other less malignant cell group is identified at the same time. In the 6 cases in which surgically removed tissue was available, this requirement was met twice. Immediate diagnoses were made from tissue obtained by small biopsies in 3 and by subtotal excisions in 3. Glioblastomatous tissue was recognized once in each group. It is fair to conclude, despite the small size of the group and because of a 66 per cent error, that accurate operative histology requires more tissue than is obtainable from any removal smaller than that of a wide spread excision. All these first diagnoses (made while the patient was being operated upon) were made on fresh tissue examined either after supravital staining of a smear or after frozen section, or both. That the dual nature of these tumors was not recognized at this time was due partly to the concentration of the pathologist on making a single definite cellular diagnosis but chiefly to the small amount of tissue that was provided him. It was not until after more material was obtained by autopsy or a more prolonged study of a greater number of fixed sections made that the multiplicity of types was recognized. It seems reasonable to conclude therefore, that the accuracy of the histological classification of an intracranial glioma, even if not extended beyond the point where the only requirement shall be a certain recognition of the presence of glioblastomatous and medulloblastomatous tissues, increases directly with the amount of tumor tissue made available by the surgeon and studied by the pathologist.

#### SUMMARY

The classification of intracranial gliomatous tumors as proposed by Bailey and Cushing cannot be considered satisfactory or final at this time. If adhered to, it has been found possible to demonstrate in individual tumors cells from either extreme of a given family tree or from different families altogether. In the absence of any classification as good however, it is preferable to use it at this time and, as a result, to consider the glioblastoma and medulloblastoma as histologically the most malignant and unfavorable types and the astrocytoma and ependymoma as the most benign and favorable types of the common intracranial gliomas. On that basis, it must be conceded that the therapy and prognosis of any given

intracranial glioma will depend on the ability of the pathologist to recognize in biopsied specimens and during the operative procedure, the presence of glioblastomatous or medulloblastomatous tissue, more accurate classification being reserved for later study. Furthermore, it appears probable that any intracranial glioma that contains either of these two cell groups has, for practical purposes, a life expectancy of about a year and that the operative risks must be assayed accordingly. Such risks should include not only the chances of death on the table but the even more important chances of life with complete disablement. The accuracy of the pathologist's diagnosis and therefore the amount and efficiency of the surgeon's therapy varies directly with the amount of tumor tissue available to and studied by the former at the time of the operation.

#### CONCLUSIONS

About 11 per cent of intracranial gliomatous tumors are of truly mixed type.

A patient with an intracranial gliomatous tumor, as far as we know now, that contains either glioblastomatous or medulloblastomatous tissue will have, with only rare exceptions, a life expectancy of not more than about 1 year.

Surgeons should not expect and pathologists should not give an opinion as to the degree of malignancy of a given intracranial glioma without the proviso that its accuracy varies directly with the amount of tissue provided by the one and studied by the other.

Surgical therapy of intracranial gliomatous tumors should be conditioned as much by the demonstration by the pathologist during operation, of glioblastomatous and medulloblastomatous tissue, as by the accessibility of the tumor that is to be removed.

We wish to thank Drs Leslie S. Jolliffe and G. Kenneth Mallory, both of the Mallory Institute of Pathology of the Boston City Hospital, for preparing the photomicrographs.

#### BIBLIOGRAPHY

1. BAILEY, PERCIVAL. *Intracranial Tumors*. Pp 216 et seq. Springfield, Illinois: Charles Thomas, 1933.
2. CARMICHAEL, E. A. Cerebral gliomata. *J Path & Bacteriol*, 1928, 31: 493.
3. GLOBUS, J. H. Die Umwandlung gutartiger Glome in boesartige Spongioblastome. Ein Beitrag zur Frage der sog. Geschwulste des Nervensystems. *Ztschr f d ges. Neurol u Psychiat*, 1931, 134: 325.
4. GLOBUS, J. H., and STRAUSS, I. Spongioblastoma multi forme, etc. *Arch Neurol. & Psychiat*, 1925, 14: 139.
5. LEVINE, G. Some transitional gliomas. *Am J Cancer*, 1939, 35: 22-37.
6. PENFIELD, W. Classification of gliomas and neuroglia cell types. *Arch Neurol. & Psychiat*, 1931, 26: 745.
7. SCHERER, H. J. The forms of growth in gliomas and their practical significance. *Brain*, 1940, 63: 1-11.

## JUVENILE KYPHOSIS

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THE orthopedist constantly sees children with rounded shoulders and poor posture. Quite often a patient is presented by the parent seeking advice for one of two reasons—posture or pain and fatigue. Ache and fatigue in children between the ages of 10 and 17 years, when present in the dorsal spine, demand careful investigation. For a number of years the hollow-rounded back of adolescents has interested us.

The clinical condition of juvenile kyphosis is not as rare a disease as formerly thought. In the last two decades the literature has grown to quite a volume, the majority of contributions having appeared in foreign publications.

Schanz first suspected that posterior curvature developing in children did not wholly arise from poor posture in school but had a more serious background. He believed the kyphosis of adolescents was the result of heavy work and unusual demands on the back. Scheurmann, in 1921, described the term *kyphosis dorsalis juvenilis*, publishing his clinical and roentgen interpretations of the irregular outlines of the vertebral bodies. Schmorl, in numerous publications of his anatomical and pathological studies, has given us his conception of the vertebral changes. Haas in the past year has added pertinent studies in regard to growth of the vertebral column and epiphyseal changes resulting from injury.

For the past 6 years particular attention has been paid to children with dorsal back pain and kyphosis. They have been followed carefully and the treatment has been supervised as closely as possible under the orthopedic department.

It is our purpose in this presentation to review briefly the clinical picture of juvenile kyphosis, speculations as to etiology, pathology and treatment with a few personal additions in the management, which we believe have been an aid in handling these children.

### ETIOLOGY AND INCIDENCE

Many hypotheses regarding etiology have been advanced, what the true etiological factors are, however, is impossible to state definitely. The problem of balance between the capacity of the spine and functional demand is an important factor in each individual case. The use of the

term "functional demand" is based on the evaluation of physical demands made on the individual in relation to the economic status of the home, number of children in the family, rural or urban environment, physical work, labor laws, and educational demands. The capacity of the spine implies tolerance to physical exertion at any stage in its development and must include the factors of growth, diet and protoplasm.

From a clinical standpoint four possibilities present themselves: (1) abnormal functional demand plus normal back—juvenile kyphosis; (2) abnormal functional demand plus abnormal back—juvenile kyphosis; (3) normal functional demand plus normal back—0; (4) normal functional demand plus abnormal back—juvenile kyphosis.

Statements one and two seem self-explanatory if one accepts developmental defects such as malformations of the vertebral body, malposition of notochordal structures, and endocrine disturbances. Schmorl is of the opinion that there are abnormalities not evident particularly in the cartilaginous stage of development which, under stress and strain of greater functional demand, become clinically pathological. Statement three must be considered as a possibility. However, with no abnormal elements present a pathological picture can hardly be expected to develop. Statement four is a combination of factors which we believe may produce the clinical entity. This patient is a small part of the group and usually presents no pain, ache or fatigue. Posture only is poor. These children appear in the non-indigent class and no abnormal demands could be determined during the daily routine.

From a study of 50 cases, the most frequent age of onset was found to be between 10 and 12 years (Fig. 1). Contrary to some observers, the incidence was found to be greater in girls (78 per cent). This observation coincides with the pre-dominance of females as recorded by Burns and Ellis in the Royal National Orthopaedic Hospital and with the figures of Schuklbach of Leipzig. The incidence peak is highest earlier in girls, being reached at 12 years and in boys at 14 years. In appraising the body types of these children it was found that the tall, thin child of the asthenic constitution appeared twice as frequent as the short, stocky, pyknic individual (Fig. 2). The

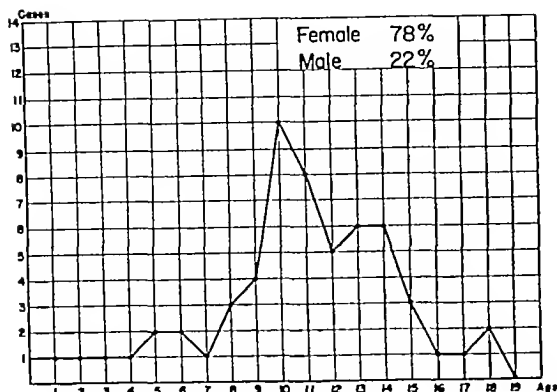


Fig 1 Incidence

majority of patients presented themselves under 6 months after the onset of symptoms—smaller groups sought advice from a year to 18 months following initial symptoms (Fig 3). From the time element it would appear that the symptomatology in these children is not alarming nor is it of a severe nature in regard to pain or acute discomfort.

#### PATHOLOGY

Prior to anatomical investigations, the changes of the vertebral column in juvenile kyphosis were largely interpreted from the roentgenogram. Scheurmann in 1921 described the changes in adolescent spines from the roentgenogram, pointing out the increased dorsal curve and wedging of the body. Shanz before him speculated on the factors back of these changes early in 1907.

Numerous publications by Frejka, Mau, Calve and Galland, and Meyer described the clinical picture and development of deformity. All these authors turned in part to Schmorl's anatomical dissections and Scheurmann's interpretations for explanation of the changes occurring within the disc and vertebral body. These investigators carried out extensive studies of the spine and came to definite conclusions as to the development of the pathological picture. Schmorl's theory propounds the herniation of the nucleus pulposus into the vertebral body causing reactive changes and cessation of bone growth. Scheurmann believed the primary change not a nuclear herniation but erosion of the anterior corners of the bodies, and also states that nuclear herniations are not always present. Cloward and Bucy reviewed cases of extradural cysts of the cord in which kyphosis was present. These cases occurred in children, and so consistent were the findings that coincidence appeared out of the question. The explanations

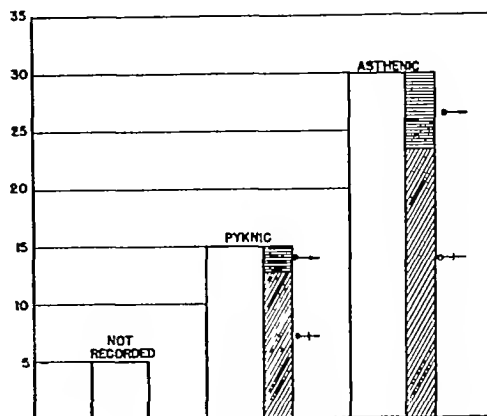


Fig 2 Constitutional type

offered in relationship of the cysts to development of kyphosis may spread some light for future investigation. Their theory states that venous stasis and congestion within the ventral body may be a contributing factor. All these writers have attempted reasonable explanations for the changes, but there still remains much controversy. One cannot possibly outline the various individual conceptions in this short review, however, the general conception of the changes can be sketched here.

Anatomically, the intervertebral disc consists of three distinct parts, the annulus fibrosa, the nucleus pulposus, and the two cartilaginous end plates which form the inferior and superior coats of the disc.

The annulus is a fine fibrous network running in oblique planes covering the anterior lateral and posterior borders of the discs. It completely encircles the intervertebral disc substance and is

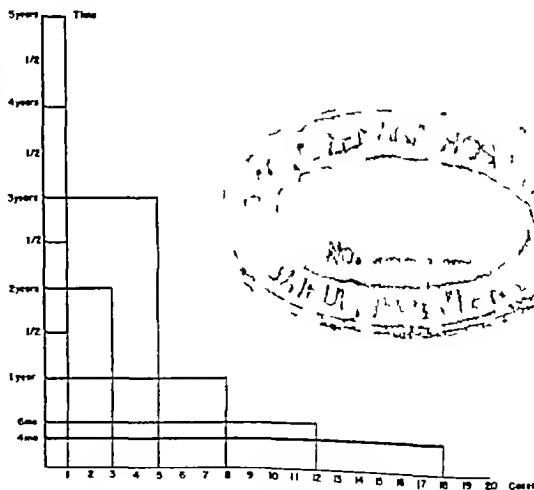


Fig 3 Duration symptoms prior to treatment

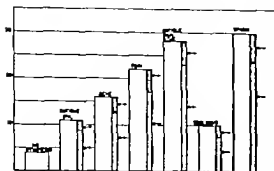


Fig. 4. Symptoms and signs.

attached more loosely in the dorsal or posterior aspect. The peripheral edges of the annulus send fibers deep into the marginal ledges of the vertebral body. The fibrous networks of the annulus pass gradually centralward becoming less dense and less compact, gradually merging into the nucleus pulposus which is partly myxomatous and partly fibrillar. In youth the pressure within this structure is greater than in the aged. Petter found that, on removal from the body, the intervertebral disc expands and a pressure of some 30 pounds is necessary to reduce this expansion. Evidently this pressure is due in part to water content. In the youth there exists 80 parts of fluid as in contrast to the aged where only 60 parts fluid is present.

The cartilage end plates are thin rigid structures of hyaline cartilage forming the superior and inferior surfaces of the disc. They do not reach the outer visible margin of the disc but end on the inner marginal ledge of the corons, which will be mentioned below.

The tension within the nucleus is maintained by the lamina and cartilage end plates. Schmorl removed a bony vertebral body from the disc being careful not to injure the cartilaginous end plate and found that the tension within the intervertebral disc did not change. He concluded, therefore, that the cartilaginous end plates must be an important factor in maintaining tension. Evidently then the cartilage plate is as intimate with the disc as with the vertebral body.

If for some reason the resistance of the cartilaginous end plate is below normal, changes in tension may occur by herniation of nucleus thru small splits in this end plate. Whether these fissures or interstices develop from strain or trauma, or weakened areas exist as the result of involuted nutrient vessels from an earlier age, cannot definitely be stated. The abnormalities may remain within the bounds of clinical normalcy

and assume a pathological character only under the stress and strain of increased functional demand on the disc. It is from this basis that we mentioned the four statements or combinations possible in developing the clinical entity.

It is believed that under increased demand zigzag fissures appear in the cartilaginous plates, allowing nuclear material to herniate into the spongiosa of the vertebral body. The pressure of the nuclear substance further tears and enlarges the fissures allowing a greater mass to come through. Reactive changes develop around these cartilage nodules in the spongiosa of the vertebral body. By release of tension the width of the intervertebral disc is lessened and the cartilaginous plates approach each other. In areas in which the perforations occur through the bony end plates of the vertebral body the cartilage proliferation zone is destroyed and bone growth ceases. This is the case at the ventral or anterior portion of the vertebral body when greater pressure is exerted.

The delay in growth is shown as narrowing of the anterior body producing the picture of wedging. Defects in the ossification are seen along with irregular broadening of the cartilaginous proliferation zone.

Schmorl apparently objects to the term vertebral epiphysitis as used by Scheuermann in designating the ossification line as an epiphysal line. He stated and was supported by Virchow that the so called secondary epiphysitis is not a growth epiphysitis in the same sense as long bone. The vertebral body develops by endochondral bone growth on the spongiosa side of the cartilage end plates. One may be justified in speaking of this as a growth zone and not an epiphysitis, thus, discarding the term vertebral epiphysitis. Haas, however in experimentation on dogs concluded that the growth in length of vertebrae occurs in manner similar to growth in length of long bones, a proliferation at the cartilage end plate with no interstitial growth within the body. If produced both kyphosis and scoliosis by injuring these plates surgically. These variants in conception of growth do not change the ultimate result. The nuclear substance under pressure, whether destroying the cartilage proliferation zone of Schmorl or the cartilaginous epiphysal cells according to Haas, interrupts the growth anteriorly to produce wedging or lateral changes may produce a scoliosis.

Freijla seems to stress the possibility of nasal obstruction playing an important rôle in the development of kyphosis. Children with large adenoids and tonsils breathe through the mouth, such respiration is shallow and there is a more or less constant condition of expiration in the thorax. A

constant condition of this description causes a change in posture and in the general form of the spine and thorax. The chest is dropped and slumping occurs. The increased curving of the dorsal spine increases pressure within the discs.

In the near past roentgenologists frequently assumed that a disease of the epiphysis existed because this area was seen as a hazy and indistinct or irregular outline. These areas may be interpreted as irregularities in ossification interrupted by passage of nuclear substance through the end plate into spongiosa.

In the adolescent spine one finds about the periphery of the bony end plate, a cartilaginous ring. During the period of growth small areas of calcification or ossification appear within this ring and as time goes on these areas become confluent finally to present a bony ring. This ossifying or calcifying ring may be seen roentgenologically in its different stages of development. This picture will be referred to later in conjunction with roentgen diagnosis.

In brief summary of the development of these changes one may say that the destruction of the growth zone or epiphyseal cartilage zone may be caused by herniations of the intervertebral disc with resultant decrease in growth anteriorly in the vertebral body. While we have seen clinical kyphosis in the adolescent without radiological evidence of nuclear prolapse and again multiple nuclear herniations without kyphosis, we are sure that the nuclear herniations and cessation of growth of the body anteriorly are important considerations in the development of juvenile kyphosis.

#### CLINICAL PICTURE

Patients presenting themselves for examination do so usually for two reasons: poor posture or ache and pain in the back. A slumping posture has been noticed for a number of months and the child has complained of backache. On the other hand, the parent suddenly discovers the child has a badly rounded back and seems easily to become fatigued.

Ache or pain with fatigue are present in the majority of cases (Fig 4). It is this symptom which brings attention to the back even in absence of curvature. The individual has a dull aching in the mid dorsal or low dorsal region, the severity of which may vary from a feeling of fatigue to aching and actual radiating pain on exertion. At times, the complaint of chest pains may be elicited with a "crowded" sensation in the thoracic cage. Many times the child is content to come straight home from school and rest at his own initiative rather than run and play after

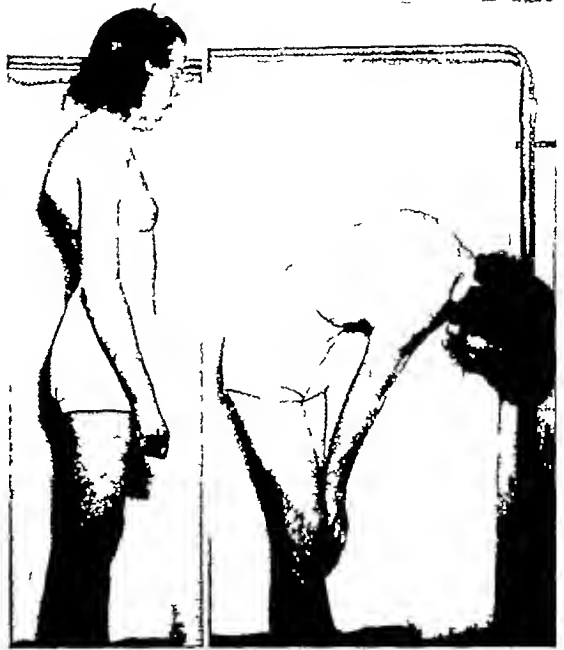


Fig 5 a, left Shows posture with increased curve dorsal spine. Head carried forward. b, Shows in forward bend the arcuate curve in mid and high dorsal spine.

school hours. This act of voluntary rest points to fatigue and is present at times without evident postural changes in the dorsal spine.

A greater percentage of children with back complaints are of the tall, ungainly type (Fig 2). They have "sprung up overnight" so to speak in their growth. It has been our experience that these children complain of aching more than fatigue.

On examination one observes a rounded back accentuated by a slump of the shoulders. The head is carried forward, thus accentuating the contour of the dorsal spine. The chest is more or less flattened and plays a minor part in breathing. The abdomen is relaxed and abdominal breathing is pronounced. This picture is more in evidence in the tall individual (Figs 5a and b). Increased lumbar lordosis in association with hyperextension of the knees and pronated feet completes the picture.

Palpating the dorsal spine one seldom elicits localized areas of pain or tenderness. Sharp tapping over the low dorsal spine with the heel of the hand may cause the patient to complain of pain especially in the forward bend position. The erector spinae group may exhibit spasm in the lumbar and dorsal spine equal bilaterally.



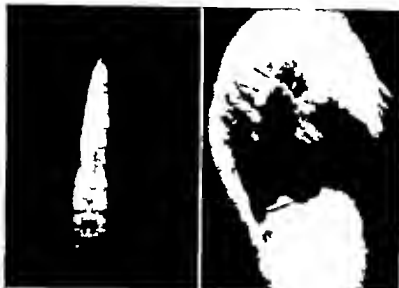


Fig. 6. a, left. Anteroposterior projection, shows paravertebral thickening. b, Lateral projection, shows increased dorsal curve, edging of bodies, densification of bony substance with reactive changes in bodies, and decreased intervertebral disc space.

The forward bend position accentuates the arcuate curve of the dorsal spine. Those individuals with tenderness bend slowly and with splinting action of the erector spinae group. This protective mechanism is clearly seen in the attempt to gain the erect position from the forward bend attitude. *The erect position is gained by first straightening the dorsal spine on the fixed lumbar spine. Following this maneuver the entire trunk is brought into extension.* This is a definite segmental movement as contrasted to the usual supple co-operative extension of all the segments of the normal spine and is our experience a diagnostic sign from a clinical standpoint.

The patient with a rigid back on attempt at side bending, and torsion does so with the hips, the lumbar spine acting in a minimal capacity. Hyperextension is a protected movement. Less rigid backs will perform these maneuvers in an almost normal fashion except for the segmental movement on gaining the erect posture from forward bend.

The spasm of the erector spinae is more evident in the dorsal and dorsolumbar regions. The musculature is tight and not infrequently tender to pressure. The lumbodorsal fascia may be contracted thus contributing to the lordosis. Hyperextension of the knees and relaxed or pronated feet are common. The pronated foot is observed at a 45 degree angle or greater. Seldom do the feet plant themselves parallel, in assuming a posture.

Unilateral tightening of the hamstring muscles has been credited for scoliosis. We have observed scoliosis in a small percentage of these children (Fig. 4) but have to date seen only one case of tightened hamstrings, bilateral. The kyphoses observed with a scoliosis have not shown roentgen evidence of abnormalities that may be said to be the cause of the lateral curve. One may find, of course, other changes of a congenital nature in the vertebral bodies that may accompany the kyphosis and produce the scoliosis. The logical explanation is the interruption of growth laterally as well as ventrally. The scoliosis may be either to right or left and is not severe. The rotation is away from the convexity.

The typical picture then is that of a generally rounded back with limited mobility, relaxed abdomen, increase in lordosis, and hyperextension at the knees. So far in our experience we have not seen the severe rounded kyphosis as depicted in foreign publications. Some of these approach the angular kyphosis. It is not logical to assume that the capacity of the spines of European children is less than our own children. However, the demands made upon the backs of the European child may well be greater during this child's growing period. The economic status of this country and that of Europe differ greatly. More physical labor may be demanded of the child in Europe than in our own States.

## ROENTGEN FINDINGS

The generally accepted criteria necessary to make a diagnosis of juvenile kyphosis are (Fig 6)

- (1) increased dorsal curve, (2) anterior wedging of the vertebral bodies in the dorsal region, (3) diminution of the intervertebral joint space, (4) serration of the anterior surfaces of the bodies, (5) nuclear herniations into vertebral bodies, (6) paravertebral thickening

The increased dorsal curve as seen in the lateral projection is a generally rounded arc, the anterior vertical height of the vertebral body less than the posterior vertical height. This wedging plus the narrowing of the intervertebral spaces produce the exaggerated curve. These findings occur in the low dorsal spine, usually from the seventh dorsal downward. Changes higher up are, however, seen.

Wedging of the bodies is due to arrested growth anteriorly. In the lateral projections the superior or inferior surfaces of the bodies may exhibit an arc-shaped or semicircular area of rarefaction immediately beneath which is found a circular zone of increased density due to irritative bone production. The escape of nuclear substance into the spongiosa releases tension within the intervertebral disc thus allowing collapse and the resultant picture of decreased intervertebral space.

Saw-toothed serrations of the anterior borders of the vertebral bodies are said to be the result of pressure phenomena exerted on a softened vertebral body. These serrations appear at the metaphyseal areas superiorly and inferiorly. One hesitates to accept the explanation of softened bone structure as we believe the vertebral body not primarily involved in the pathological process.

The irregular punched out areas seen on the superior and inferior anterior surfaces, so called "saw cuts," are not a part of the roentgen picture in arriving at a diagnosis. On the contrary they are calcifying or ossifying areas of the "corona" about the vertebral body in different stages. This is a picture of normal development.

Paravertebral thickening in the anteroposterior projection is described by Brailsford. This thickening runs along the lateral borders of the spine in the area affected. The significance is not definitely understood.

In the late stages one may see secondary arthritic changes. The close approximation of the vertebral bodies resulting from the collapsed disc may allow bridging. Lipping of margins may develop.

## TREATMENT

Treatment naturally seeks to bring an end to symptoms and arrest or correct the existing de-

formity. Fundamentally, one attempts to establish a balance between the capacity of spine and functional demand. This balance is established during actively supervised treatment, namely by support, rest, and limitation of activity.

One may arbitrarily divide the treatment into three stages: (1) the period between the time the diagnosis is made to cessation of ache, pain, or fatigue, (2) from the cessation of symptoms to return to work and activity or, normal range and exertion, (3) from this point of activity to cessation of the growth period. It may be well to state that, in some cases, one may not get a patient to normal range of activity in the second stage, and it is only when the growth is complete that the individual reaches a normal sphere of activity. In other words, there is no second period here.

It is our belief that one cannot expect to change the general contour of a wedged vertebra when once developed. However, one can expect better posture and stronger spinal musculature under treatment. The clinical complaints of ache and fatigue are alleviated by adequate rest and support.

On arrival at a diagnosis the patient is placed at rest. By rest is meant flat in bed, being up only for a short time as demanded by meals and bathroom privileges. No other time periods are allowed the first 30 days. The bed should have a hard or firm mattress. The inner spring mattress is not tolerated. Boards placed longitudinally beneath the mattress and on the springs suffice. If there is a fair degree or well developed kyphosis, the child is fitted to a plaster-of-Paris shell.

The shell is made with the patient on his abdomen. The body must be straight on the table and a pillow under the abdomen to obliterate the lumbar lordosis. Plaster bandage is laid across the back, carried to the midaxillary line laterally and extends from gluteal crease to base of the scapulae. After 5 or 6 layers, a re-enforcing strap iron is placed in the long axis over these layers, having been bent to the contour of the back. These are incorporated with 4 or 5 more layers. Canvas strap is also incorporated to cross the shoulders and circle the abdomen to facilitate holding the shell snugly to the body. It is well to remember that this shell must be molded carefully about the hips and held snugly here while setting. After the setting the upper portions beneath the axillae are shaved down so that there is free movement of arms and no pressure dorsally to crowd the shoulder girdles ventrally. The shell after this process is then filled in with plaster cream in the dorsal portion which exhibits the

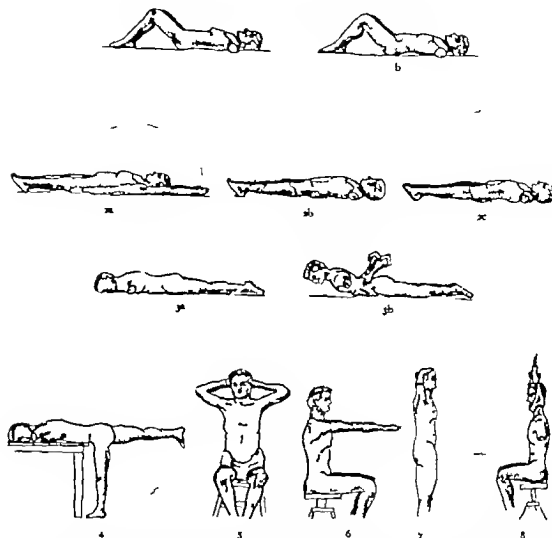


Fig. 7. Exercises for cervical hypsosis.

Back lying—*a* and *b*. Knees slightly flexed, abdominal retraction and flattening of lumbar spine for the count of three.

Back lying—*a*. Legs extended and arms at side, lumbar spine flat. Extended arms forward over head in arc-like manner keeping the lumbar spine flat. *b*. Legs extended and arms at side, lumbar spine flat. Bring legs into flexion keeping lumbar spine flat, relaxing down to extension maintaining the lumbar spine flat. Legs extended and arms at side with lumbar spine flat. Raise leg, left knee in extension and foot at right angle to leg. Slowly descend to extension, left lumbar spine flat.

Note: These exercises must be done on a flat hard surface.

1. Prone lying—*a*. Arms at side extension of dorsal spine from prone position. Attendant's hand at high lumbar spine so that only dorsal spine is exerting extension (preventing lordosis). The head must be held in extension with

the chin in (not hyperextending the cervical spine).

4. Table lying—prone. Flexion at thigh, arms in extension, extending legs holding lumbar spine flat, alternate extension of legs.

5. Sitting back to all. With hands clasped back of head, circumduction of shoulder girdles.

6. Sitting back to all. With arms parallel to ground, overhead extension maintaining erect and extended lumbar spine.

7. Standing exercises. Arms clasped back of neck. With lumbar spine flat, forward bending. With legs, maintaining lumbar spine and dorsal spine in extension.

8. Sitting. Sayre head sling stretching.

Note: These exercises are to be given beginning approximately at 6th month and going up, keeping beneath the level of fatigue and discomfort. Patient gradually, working into the table flexion sitting, and standing exercises from initial back, lying and prone lying exercises.

greater kyphotic point. It is well not to fill in completely to give a flat surface initially, gradual obliteration of the kyphotic impression can be accomplished over a period of 1 to 2 months without discomfort to the patient.

Some children will not tolerate this plaster mold over an hour a night in the early periods of treatment. Usually it is the patient with spasm. This condition is met by baking twice daily for 30 minutes followed by mild relaxing massage. When physiotherapy is available it is carried out in a regular schedule. Next best is teaching the parent the technique of massage and baking at home. We are convinced that the physiotherapeutic measures have much to do with the relief of symptoms, and in these cases exhibiting spasm, are just as important as rest.

The competent physiotherapist working daily with a patient will determine the gradual disappearance of spasm in the erector spinae group and in conjunction with the attendant, arbitrarily determines the gradual increase in activity. If after a month the back is free of ache and is more or less loosened up, the child is allowed periods of supervised activity. These may be 1 or 2 hours in the mid-morning and the same period in mid-afternoon. Between times the patient continues to remain at rest in the shell.

At this period are begun exercises in addition to the bakes and massage. Initially, they are back lying and prone maneuvers to be described. They are supervised by the physiotherapist who can gauge the time and vigor of the exercises, gradually adding to the routine.

As the child develops tolerance and strength, standing exercises are brought in, and, when the patient fully understands the routine, he is allowed more time and activity.

In those patients with a well developed kyphosis wherein the posture does not correct, a spinal brace<sup>1</sup> is applied. It is constructed high in front with pressure points just below the clavicles and low in back. These patients earlier in the treatment, after a month of rest, may be placed in a plaster-of-Paris body cast molded high in front and low in back. We have made it a practice of keeping this cast on a child from 3 to 6 months, changing plasters each 2 months as necessary. Not infrequently a semi-permanent celluloid jacket is used.

The ambulatory case, when an out-patient, continues his exercises and wears the shell nights. If in a brace, this same routine continues. In cases in which carriage and posture are now the only problem, the massages and bakes are discontinued.

On the patient is placed the responsibility of exercises and the wearing of the shell at night.

How long restricted activity continues and to what degree, depends upon posture and the clinical picture of the back. These factors are determined only by repeated clinical examination. In our experience repeated x-ray examination has been of no practical value over short periods of time (under 6 months). If after 6 to 18 months the posture remains satisfactory and there are no complaints, the plaster or spinal brace is removed half days. It is during this period that a discrepancy may arise between the capacity and function, the continued absence of symptoms, laxity on the part of the patient and parent may allow too much activity and symptoms return. The conscientious patient progresses without pain and the support is removed completely.

A year to 18 months in a brace is not excessive, and in children of 12 to 15 years 3 or 4 years is not unusual. As the patient grows and develops a greater muscular capacity, his activity increases and gradually he enters the sphere of normal exertion. Stage three continues up to cessation of the growth period, and the properly supervised individual will keep his carriage and posture through this period.

It is interesting to note that our foreign contemporaries have an advantage in handling children. The regimentation of the child in large clinics is an accepted fact and classes are held daily with obligatory attendance. The classes are uniformly carried out with specified exercises and over long periods of time. We are of the opinion that if these adolescents are not protected from themselves until they fully appreciate their condition or until the full growth is attained, they are sowing seeds of chronic indefinite low grade backache of later years.

#### CONCLUSIONS

1 Juvenile kyphosis is a clinical entity of not uncommon occurrence. It is seen most frequently between the ages of 10 and 14 years, females predominating.

2 The true etiology is not definitely understood.

3 Roentgenograms reveal a characteristic picture.

4 Juvenile kyphosis is a self-limited disease. Treatment aims to alleviate symptoms and arrest the deformity through rest, physiotherapy, and temporary spinal support.

5 Juvenile kyphosis, if not properly treated may lead to chronic backache and to permanent deformity.

<sup>1</sup> Described in Chapter 3 Jordan's Orthopaedic Appliances (13)

## BIBLIOGRAPHY

- BOHRETTEN. Osteochondritis of the spine. *J Bone & Joint Surg.* 1927 9, 630-635.
- BRATTLEFORD, JAMES F. Radiology of Bones and Joints, 295-357. Baltimore: William Wood & Co., 1934.
3. B. CHENAK, JOSEPH. Résumé of osteochondritis. *Surg., Gynec. & Obst.* 1930, 40-447.
4. BOY, P. C. and CLOWARD, R. B. Spinal extradural cyst and kyphosis dorsalis juvenilis. *Am. J. Roent. genol.* 1917 33, 681-706.
5. BUCKA, H. H. and ELLIS, V. H. Recent Advances in Orthopaedic Surgery. 82-83. Philadelphia: P. Blakiston, Son & Co. Inc., 1937.
6. CALVE and GALLARD. The intervertebral nucleus pulposus; its anatomy its physiology its pathology. *J Bone & Joint Surg.* 1930, 535.
7. DUEMO, F. P. Juvenile dorsal kyphosis. *Arch. de med. chir. y especial.* 1915, 33, 36-271.
8. FRIEJA, B. Infantile kyphosis. *Rev. d'orthop.* 1919, 5, 9-24.
9. Idem. Adolescent kyphosis. *J Bone & Joint Surg.* 1924, 4, 345-354.
- HAAR, S. L. Experimental production of scoliosis. *J Bone & Joint Surg.* 1930, 1033-1038.
- Idem. Growth in length of vertebrae. *Arch. Surg.* 1930, 35, 245-249.
2. HARRIS, M. and LULLYMORE, R. Osteochondritis of the growth centers. *Surg. Gynec. & Obst.* 1910, 5, 145.
3. JOHN, H. H. Orthopaedic Appliances. New York: Oxford University Press, 1930.
4. MEYER, MARCEL. La cyphose douloureuse des adolescents son substratum anatomique. *Rev. franç. de pédiat.* 1932, 8, 155-5.
5. SCHWAB, A. Schule und Stübchen. *Jahrb. f. Kinderh.* 1902, 27, 26.
6. SCHWAB, W. H. Kyphosis dorsalis juvenilis. *Ztschr. f. orthop. Chir.* 1904, 4, 305.
7. Idem. Roentgenologic studies of the origin and development of juvenile kyphosis together with some investigations concerning vertebral epiphyses in man and animals. *Acta orthop. Scand.* 1934, 5, 6-6.
8. SCHWAB, GEORGE. Pathogenesis of juvenile kyphosis. *Fortschr. a. d. Geb. d. Roentgenstrahlen.* 1930, 4, 319-323.
9. SCHULDRACH, JOSEPH. The development of juvenile kyphosis. *Zentralbl. f. Chir.* 1937, 36, 2046-2047.

# THE RESULTS OF SPLENECTOMY IN GAUCHER'S DISEASE

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IN 1882 Gaucher described the splenomegaly which bears his name. He considered it a primary tumor of the spleen, but later investigators, notably Pick (22), Mandelbaum, and Epstein have shown that it is due to a disturbance of lipid metabolism, resulting in the deposit of kersin in the cells of the reticulo-endothelial system.

The clinical features of the disease are a progressive splenomegaly, a tendency to hemorrhage, brownish yellow discoloration of the skin, and wedge-shaped pingueculae. As the Gaucher cells develop in organs other than the spleen, they give rise to secondary clinical types. An osseous form of Gaucher's disease has been described by Pick (23). Destruction of bone with fracture or deformity occurs in about half of all cases. Neurological signs may predominate, especially in infants (1). Lesions of the lung (19) and kidney (14) have been described. The liver enlarges more slowly than the spleen, and a late cirrhosis may occur. Lymph nodes are occasionally enlarged.

The blood picture is not striking. There is a mild anemia with leucopenia. The differential count is normal. The thrombocytes are often reduced, but the bleeding and clotting time are normal. The fragility test is normal.

Diagnosis can be made from examination of the bone marrow by sternal puncture (33), which has displaced the dangers of splenic needling. Biopsy of an enlarged lymph node revealed the diagnosis in the cases reported by Hoffman and Makler and Donovan. The Gaucher cell is a large endothelial cell with grayish white cytoplasm containing fibrillae. The nucleus is small and eccentric. The cell contains the lipid kersin, a cerebroside.

The disease is familial, congenital, and possibly hereditary. Anderson has suggested that it is transmitted by unaffected males. (My own case lends some support to this idea.) Although it appears to have a predilection for the Jewish race, it occurs in members of all races, including negroes (13, 29) and orientals (31). Contrary to former belief, the sex incidence is about equally divided between males and females. Atkinson analyzed 103 cases (children) of whom 53 were females and 50 males.

Gaucher's disease usually becomes established early in life, but the progress of the illness is so chronic in some cases that it escapes notice until

long after maturity. Siegmund's case, quoted by Hoffman and Makler is the youngest patient on record, being 1 week old. Wechsler and Gustafson recently reported a case in a woman 71 years of age. Horsley and his associates found in a study of 71 cases, that over half of them were recognized before the age of 8 years.

Death usually results from intercurrent infection, often pneumonia. Melamed and Chester's patient, and Ullrich's also, died of the osseous form. Rowland and Aballi and Kato have called attention to an acute, fatal, infantile form with neurological symptoms.

Gaucher's disease is closely allied to the other disorders of lipid metabolism. These are Niemann-Pick disease and Hand-Schuller-Christian disease. Tay-Sachs disease (congenital familial amaurotic idiocy) is now considered to be a cerebral form of Niemann-Pick disease. These "xanthomatoses" have been amply discussed by Pick (22).

There is no specific treatment for the disease. Potter and McRae felt that liver extract helped one of their patients, but there has been little subsequent enthusiasm for this suggestion. X-ray radiation over the spleen had no retarding influence on the growth of the organ in either Pick's case or mine. In both cases it produced anemia, and therefore it seems to me to be a harmful treatment. Splenectomy, which was first performed for Gaucher's disease in 1895 (24), remains the most hopeful palliative measure. The principal objection to the operation is its high mortality. There is a conviction, possibly based on the first 10 recorded splenectomies for Gaucher's disease (11) that the operative risk is 20 per cent, since 2 of the 10 patients succumbed. Atkinson states that 7 of the 47 children, who had had splenectomy for Gaucher's disease, died after operation. This suggests a mortality rate of about 15 per cent in children. Whipple reported but 10 deaths in 106 splenectomies performed for various reasons in his Spleen Clinic at the Presbyterian Hospital. Since the Gaucher spleen, while enormously large, is one of the easiest spleens to remove, owing to the fact that it is rarely adherent, the current mortality rate must be much less than 20 per cent.

The immediate effect of splenectomy in exsanguinated children is often miraculous. Both

Myers (19) and Ulrich's infants were essentially moribund prior to operation. Several authors, including Moeller have felt that splenectomy hastened the rate of bone involvement. However de Lange who had followed two sisters for 9 years, observed that the skeletal changes were less marked in the splenectomized girl, although both children had lesions of the hip and tibia.

Indications for splenectomy are hemorrhage (especially when the platelet count falls below 100,000) and the discomfort of a large abdominal tumor. In Pool's case (25) the compelling reason was a desire to bear children, as the first pregnancy had terminated in a miscarriage. Hunter and Evans reported that their patient had 3 miscarriages, attributed to the enlarging spleen.

Late reports on splenectomized cases are unfortunately rare. For this reason I am reporting a new case 7 years after operation, and shall present notes on the present status of several well known cases previously described in American literature.

#### REPORT OF CASES

A S. young unmarried woman, 28 years of age, was referred to us in January, 1931, by Dr. Bernard Samuels because of small incision of the lower eyelid had bled for 4 days. Two years previously, she had bled overmuch after the extraction of tooth. Nose bleeds are rare but bradycardia is common. She had lost 7 pounds from dieting to reduce the size of her abdomen. No pain or dragging had been felt. She is employed in useful capacity in the office of hospital planning expert.

The family history is interesting. Her father is half Jewish, but there is no other Jewish ancestry. One of her brothers had large spleen. He was years younger than his sister and had known for 6 years (from the age of ) that his spleen was enlarged. As he lived in malarial region of Louisiana, no attention had been paid to it yet he had never had chills and fever. During the 3 years he was under observation in New York the spleen did not increase in size. His blood count in May 1918, as normal.

Physical examination of the patient showed tall, pale young woman, with small basilar incision of the lower right eyelid, oozing blood. The heart and lungs were normal. Traube's space was flat on percussion. The abdomen was full, especially on the left. A hard, smooth mass filled the entire left half of the abdomen, with notch at the umbilical level. The mass extended deeply into the left iliac fossa. The liver edge was not felt. There were several large bruised areas on the skin, and one over the thigh. Superficial lymph nodes were not enlarged. There was no pigmentation. Punguercles are absent.

The patient is quite anemic and had leucopenia, as shown in the accompanying blood tabulation. The thrombocytes count is 50,000. The blood loss is quickly made up after control of the bleeding by suture. The spleen continued to grow but there are no symptoms except fatigue. The diagnosis seemed reasonably clear for Gaucher's disease, but it was suggested that x-ray therapy be tried. This merely resulted in restoring anemia, without controlling the continued growth of the spleen. By the end of March the organ is occupying much of the right iliac fossa, having crossed the midline into the right

tion, as recommended because of the great size of the spleen.

The patient elected to go to her home in Sutterport, here on June 5, 1931, Dr. E. L. Sanderson of that city took out the spleen and sent me his operative report. "I removed the spleen, which weighed 9 pounds after removal. Of course it is much larger until tied the artery and applied gentle pressure before tying the clasp. There are no adhesions and the operation is comparatively easy. She has had an uneventful recovery. Our pathologist makes positive diagnosis of Gaucher's disease. This was also the opinion of Dr. Ralph G. Stillman of New York Hospital, to whom I submitted section of the spleen, sent by Dr. Sanderson.

Following her convalescence, the young woman came back to New York, here she resumed her work. Last year (1930) she returned to her home to look after her mother who was ill. There has been no clinical evidence of bone involvement, although no recent films have been made. Studies in 1931, about year after operation, showed minimal thinning of the cortex of the femur shafts. The blood count shows slight reduction in the red cells and persistent leucopenia, with normal differential count. On one occasion smudged red cell as seen per os late blood cells. Pigmentation and pinguercles have not developed. The patient says that she feels fine.

Pool's case. I. o. Pool (3) reported the case of young married Jewish woman, 5 years of age, who had in the past year begun to lose weight and strength. She had been explored by another surgeon, who pronounced that the cause of miscarriage was an ovarian cyst. Although the mass was identified as spleen, it was not removed. Five months later she came under Dr. Pool's observation. He found an enormous spleen, extending to the anterior superior spine on the right and almost into the pelvis.

Splenectomy was done on January 5, 1910, because the patient desired to bear children. Pre-operative studies of the blood showed mild secondary anemia, without leucopenia, while the platelet count was normal. Pathological studies of the spleen showed typical Gaucher's disease. The case is fully documented in the monograph *Surgery of the Spleen* by Pool and Stillman (28).

In 1913, 7 years later Pool (26) again reported the case. "Her health has been good, with one exception. Four years ago her left hip became painful. It was put in plaster in another hospital for 6 weeks and the joint is now movable and painless. She has decided lump enlargement of the skull and other bones show no evidence of disease except in the left hip joint, where there is definite destructive process involving the head of the femur. The head is mottled, there is definite bone absorption and irregular calcification. The greater trochanter shows decalcification process and the medullary substance in the shaft shows nothing for about two-thirds of the shaft. These changes are interpreted as the result of Gaucher's disease.

In 1920 Pool and Hipsley (27) reported that the bone changes in the hip had not progressed and that no new lesions had occurred. At this time the patient had 11 children and was expecting third.

Dr. Pool has kindly allowed me to make use of his recent notes on this woman, who is now 44 years old. Nineteen years have elapsed since the splenectomy. In the past year she has had some pain in her left shoulder. X-ray of this region shows no bone destruction, although one observer thought there is some cortical thinning. The hip has shown no further change. A sternal bone marrow puncture revealed no Gaucher cells, but seems remarkable. The blood picture is given in the accompanying table. There is no pigmentation of the skin and the liver is not enlarged. Pinguercles have not appeared. The patient looks well.

## BLOOD COUNTS, CASE A S

Date	Hb %	R B C	W B C	Poly \ %	Lymph %	Mono %	Eosin %	Baso %	Nucl R B C per 100 W B C
1 13 1932	60	2 910 000	2 800	54	42	3		1	
9-10-1932	75	4 400 000	1 400	65	11	1			

## \ ray therapy

3 15-1932	60	3 850 000	1 200	75	22	3			
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## Splenectomy June 5 1932

7 5 1933	96	4 205 000	14 150	49	42	6	3		
10-25 1933	75	3 536 000	12 500						
1 25 1938	82	4 040 000	22 000	56	37	5	1	1	
10-31 1938	106	4 100 000	24 000	57	27	11	3	2	1
10-17 1939	105	4 560 000	18 800	64	27	6	2	1	

Hb % hemo., lobin per cent R B C red blood cells W B C white blood cells Poly \ polymorphonuclear neutrophils Lymph lymphocytes  
 Mono mononuclears Eosin eosinophiles Baso basophiles Nucl R B C. per 100 W B C. nucleated red blood cell per 100 white blood cells

## BLOOD COUNTS, POOL'S CASE

Date	Hb %	R B C	W B C	Poly \ %	Lymph %	Mono %	Eo in %	Baso %
1 4 1927	82	4 000 000	9 500	60	36	3	1	

## Splenectomy January 25 1931

1 7 1929	68	3 860 000	20 100	72	24	3	1	
4 21 1930	80	4 100 000	13 500	43	51		4	2
5-6-1931	67	3 340 000	12 700	73	24	3		
5 3 1930	90	4 000 000	16 000	58	29	8	4	1

## BLOOD COUNTS, FRDMANN AND MOORHEAD'S CASE

Date	Hb %	R B C.	W B C	Poly \ %	Lymph %	Mono %	Eosin %	Baso %	Myelocytes
2 28-1912	85	6 200 000	7 000	40	40	9	1	1	

## Splenectomy June 6 1912

4 22 1913	75	5,300 000	16 000	43	47	8	1	1	
4 17 1924	75	4,480 000	12 000	48	42	4	3	1	
1926			8 000						
1930	65	3 650 000	11 750	54	42	3	1		
1 1032	77	5 600 000	19 200	43	40	16	1		
4 10-1935	72	4,350 000	19 600	55	37	8			
2 7 1936	80	4 350 000	19 125	62	27	7	3	1	
5 14 1937	65	4 250 000	27 200	54	8	34		3	1
6-22 1938	65	3 110 000	20 000	50	44	5	1		
7 31 1939	60	2 900 000	12 800	40	48	1	2		
8-29-1937	74	4 150 000	14 000	44	51	1	3	1	
1 3 1940	85	4 120 000	28 000	50	38	7	3	2	
2 27 1940	83	4 400 000	12,360	70	28	8	1	3	



Dr Paul Kendall<sup>11</sup> he did the best count, made the following comment: leukocytosis plus polikilocytosis plus toxic granulation plus. Bleeding time 14 minutes; tourniquet test slightly positive. Clotting time moderately positive. Clotting time 38 minutes (normal 0-1 minutes). Clot retraction fairly good, clot fragility quite fragile. Hematocrit 38.5 per cent, album index 0.93 prothrombin 54 per cent normal fibrinogen (normal) reticulocytes 3 per cent, platelets 600,000 nucleated red blood count in smear.

*Erasmus and Moorhead*<sup>12</sup> case 1, 94 Erasmus and Moorhead reported the case of girl, 3 1/2 years old, upon whom they had performed splenectomy for Gaucher's disease on June 6, 9. This is the tenth splenectomy for Gaucher's disease reported in the old literature. This child is the fourth in the family. Her eldest brother had developed, in the second year of his life, large liver and spleen, with anemia and leukopenia. At the age of 6 he died of fulminating pneumonia. Although an autopsy as done, he presumably had Gaucher's disease.

At the time of the girl's operation, the liver extended inches below the ribs, and the spleen reached below the umbilicus and beyond the median line. Splenectomy as performed because of progressive loss of strength. Diagnosis as confirmed by studies of the spleen. The authors' final notes are made on October 6, 9, 16 months after the operation, when the child was reported still strong.

She is now 3 years of age. The only dramatic episodes since the operation has been an appendectomy in 939, without complications, and severe fall from home in 936. This resulted in compression fracture of the body of the second lumbar vertebra, without serious sequelae. Films of the spine at this time failed to show evidence of Gaucher cell infiltration.

In 93 the liver extended to the umbilical level in the mid-clavicular line. The skin on the anterior chest wall very prominent. Mitral and aortic systolic murmurs are noted. In 939 there is transient numbness of the right hand.

While this patient cannot be considered to be in perfect health, she has not suffered from gross bone destruction nor has she developed a severe or persistent nemia. The enormous liver may portend an eventual cirrhosis syndrome. I have been unable to find any other case in the literature which has been followed as long as this one 18 years, since splenectomy. It abundantly refutes Mueller's conclusions that the outcome of all patients operated upon at a young age is death either shortly after the operation or a few years later (18).

*Pack and Silverstone's* case. In 933 Pack and Silverstone reported case of Gaucher's disease occurring in a 5 year old single Jewish woman, who came to the clinic of the

Memorial Hospital in 932. She has history of progressive enlargement of the spleen and severe epistaxis for 3 years, and as found to have large spleen and liver, mild anemia, with leukopenia, and symptomless infiltration of the upper lobe of the left lung. After an absence of 3 years, she returned in January 935, having developed pigmentation of the legs, slight productive cough, and further enlargement of the spleen and liver. She had now small hemiparesis. The blood picture revealed marked anemia, with platelet count of but 67,000. Because of the purpuric manifestations, which are obviously due to the thrombocytopenia, splenectomy as performed on May 4, 935. The spleen weighed 3300 grams.

Improvement following the operation, as striking. She gained pounds in 4 months, the liver returned to normal size, and the blood platelets rose to 130,000, with corresponding increase in all the blood cells. In spite of the clinical improvement, films of the chest showed increased infiltration. Pack's comment on the lung lesion is "the infiltration process in the left upper lobe of our case as interpreted as probable tuberculous, but in the absence of confirmatory evidence for tuberculous Gaucher cell infiltration may reasonably be considered."

Eleven months after splenectomy pain occurred in the right knee. Films at this time revealed osteoporotic changes in both femora and tibiae, with no changes in other bones. Her general health was good.

Dr Pack has kindly furnished me with recent notes on this patient. Late in 938 tubercle bacilli were identified in the sputum and since then the patient has been treated by her family physician. He reports continued small hemiparesis in spite of repeated artificial pneumothorax treatments. Gaucher cells have not been reported in the sputum.

There has been increasing involvement of the skeletal system, especially in the upper portion of the right femur.

Which showed pathological fracture in December 939. At the present time, April 8, 940, the patient is still on crutches. Films in January 940, showed osteoclastic areas in the shaft of the left humerus and destruction of the right ilium, sacrum, and pelvis. The patient is fairly anemic.

The rapid rate of involvement of the skeletal system in this patient suggests poor prognosis. However it is interesting that the right tibia, the first bone involved has shown remarkable healing power. This phenomenon has been seen in Pool's case and was also commented on by de Lange.

In spite of the finding of tubercle bacilli in the sputum since the publication of this case, one wonders whether the original infiltration, so long silent, was not due to Gaucher cell infiltration with secondary tubercular infection. Myera de

BLOOD COUNTS, PACK AND SILVERSTONE'S CASE

Date	Hb %	R.B.C.	W.B.C.	Poly %	Lymph %	Mon %	Neut %	Bas %
1-935	60	2,812,000	2,000	40	42	2	2	
Splenectomy May 4, 1935								
1-936	60	4,391,000	5,700	30	43			
10-29-39	70	3,374,000	10,300	46	35			
10-15-40	60	3,700,000	8,000	60	20	6		

scription of the lungs in his patient showed many points of resemblance to the lung lesion of this case, but without the finding of tuberculosis at autopsy Hoffman and Makler state that 8 of the 89 cases reviewed by them (including Gaucher's case) succumbed to tuberculosis. Perhaps more critical study of the lungs of these patients would have revealed Gaucher cell infiltration.

*Cushing and Stout's case* In 1929 Cushing and Stout reported 2 cases of Gaucher's disease. Dr Stout tells me that he has no further information about the first case.

The second case was that of an American woman of 33 years of age, who had suffered from childhood from severe epistaxes. At the age of 29,  $3\frac{1}{2}$  years before splenectomy, she had developed stiffening, pain, and shortening of the right hip. She had all the stigmas of Gaucher's disease. On August 26, 1924, Dr Whipple removed her spleen which weighed 1017.5 grams. In 2 months she had gained 17 $\frac{1}{2}$  pounds, pigmentation lessened, and the liver was no longer palpable. In December, 1924, the head and neck of the femur were resected and sequestrums removed. Gaucher cells were found in great numbers in these fragments. The authors' last report stated that in April of the following year the lower part of the right femur had become involved.

This patient is now 49 years old, and 15 years have elapsed since her splenectomy. She is being followed in Dr Whipple's Spleen Clinic at the Presbyterian Hospital. Data regarding this patient will doubtless appear in future publications from that source. She is moderately anemic (see Table II).

#### OTHER LATE REPORTS ON SPLENECTOMIZED CASES

De Lange, already referred to, followed two sisters for 9 years, one of whom had been operated on. She found that the liver increased in size at first after splenectomy, but in later years ceased to enlarge. Pigmentation appeared in both girls at the same ages, but later disappeared in the splenectomized girl. This observation has been made by others. Both children had destructive lesions of the left hip joint.

Mueller gave the final report of Ullrich's case. This child of 3, in 1930, was almost *in extremis* from uncontrollable nasal hemorrhage, and made a remarkable postoperative recovery, only to succumb to an osseous form of the disease, with terminal meningeal symptoms at the age of 9. The finding of an accessory spleen the size of an apple, at autopsy, was one of the features of this case.

Myers (19) in 1937 reported the autopsy findings on a child 8 years old, who had had a splenectomy in September, 1931 (20). Just prior to operation the erythrocyte count was below 1,000,000, because of three severe nose bleeds. Contrary to expectations, the operation proved life saving. The lower end of the right femur was incised for a supposed osteomyelitis in April, 1932, Gaucher cells being found in the exudate. The dorsal ver-

TABLE I —RESULTS OF SPLENECTOMY 5 OR MORE YEARS AFTER OPERATION

Author	Years after operation	Remarks
Erdmann and Moorhead	31	No bone lesions. Liver large.
Pool	19	Left hip involved 3 years after operation. Now quiescent.
Cushing and Stout	15	Right hip involved $3\frac{1}{2}$ years before operation. Now under supervision at spleen clinic, Presbyterian Hospital.
Hunter and Evans	13	No bone involvement. Occasional hemoptysis. Liver enlarged.
de Castro Freire	11	No complications.
de Lange	8	Liver enlarged. Left hip joint, left tibia involved after operation with subsequent healing.
Logan	7	No complications.
Melamed and Chester	7	Died from extensive osseous type. Involvement of bone antedated operation by 7 years.
Muller (Ullrich's case)	6	Extensive osseous invasion soon after operation. Died.
Myers	$5\frac{1}{2}$	Both femurs involved soon after operation. Died of pulmonary Gaucher cell invasion and progressive osseous destruction.
Pack and Silverstone	5	Right knee involved soon after operation with later fracture of right femur and involvement of left shoulder. Pulmonary tuberculosis.

tebral bodies and the lower end of the left femur became involved during the next 2 years. In August, 1935, the lung became infiltrated and death came January, 1937, from a terminal bronchopneumonia. Gaucher cells were found in the enlarged mediastinal and hilum glands, while the air spaces of the lung were compressed by Gaucher cells developing in the small subserous and interlobular lymph nodes. There was no evidence of tuberculosis.

De Castro Freire in 1935 made a second report of the case which he had published in 1926. This concerned a girl of 8 years of age, the first case of Gaucher's disease to be reported from Portugal. Eleven years after her splenectomy, she was planning to marry at the age of 19. The liver had not enlarged and the hemorrhagic diathesis, which had been responsible for the decision to remove the spleen, had not recurred. There had been no apparent bone involvement.

Hunter and Evans have reported one of the oldest cases on record. This woman of 60 years of age became pigmented at the age of 8 and had nose bleeds from the age of 10 onward. When she was 29 the spleen was found to be enlarged. She

TABLE II.—LATE BLOOD COUNTS OF PATIENTS WITH GAUCHER'S DISEASE AFTER SPLENECTOMY

Author	Hb per cent	RBC	WBC	Poly per cent	%c RBC	Platelets	Years after operation
Frisman and Morland	8	4,000,000	12,500	70			21
Pool	90	4,000,000	16,000	53	1 <sup>a</sup>	200,000	1
Carling and Starr <sup>b</sup>	70	3,800,000	9,000	34	4/1000	215,000	5
Hunter and Evans	67	3,000,000	8,400	65	1/1000	60,000	
de Castro Faria	66	3,100,000	3,000	40		66,000 (Spherics)	23
Logan	105	4,000,000	16,000	64	1/1000		
Melamed and Chester	48	1,000,000	8,000	40	1000/1000	90,000	6 1/2
Miseller	8	600,000	7,000	67	1/1000	75,000	8 <sup>c</sup>
Myers	87	5,000,000	73,000	65			
Pack and Silverstone	60	3,700,000	9,000	60			1

<sup>a</sup>The full differential leucocyte count is omitted because it shows no essential variation from the normal.

<sup>b</sup>Number on entry to hospital.

<sup>c</sup>Specimen from spleen tissue, Presbyterian Hospital.

<sup>d</sup>Melamed.

<sup>e</sup>14 months before death.

had 2 living children and had had 3 miscarriages. Before her spleen was removed she had begun to have hemoptyses. After the operation, performed in her forty-seventh year the abdominal pain, which was the reason for the splenectomy disappeared. Pigmentation decreased. At the time of Hunter and Evans report, 13 years after the operation, she tired easily suffered from head aches, had developed pinguiculae and again suffered from occasional hemoptyses. Signs in the lung were negative. The liver edge was 2 inches below the costal border.

Melamed and Chester in 1938 gave the final report of a 26 year old male, who had suffered from an osseous type of Gaucher's disease from the age of 13 years. When he was 20 years old the spleen was removed. He had purpuric manifestations without thrombocytopenia before the operation and was largely relieved of these for some years. In the last years of his life the bone destruction was so marked that he was bedridden. Invasion of the bone marrow finally produced a malignant anemia, which was heralded by the appearance of increasing numbers of nucleated red cells (Table II).

#### ANALYSIS OF STUDY

In reviewing these cases, one is struck by the uniform improvement in the clinical picture immediately following splenectomy. Hemorrhage is controlled, the patient gains weight, the liver decreases in size, and pigmentation often lessens or disappears. The hemorrhagic diathesis is not always cured by splenectomy. Carling and his associates found that their patient continued to

have hemoglobinuria after splenectomy. Hunter and Evans reported recurrence of hemoptyses after splenectomy as noted, and Pack's patient has had similar experiences. Ulrich's patient is reported by Miseller to have had recurrent ecchymoses 2 years after operation. In most cases, however hemorrhage does not recur and the thrombocytes maintain a normal level. The chief change in the blood picture after splenectomy is the replacement of a leucopenia with permanent leucocytosis. This is true of most of the cases reviewed in this paper. The differential count is essentially normal both before and after splenectomy. Nucleated red cells appear from time to time, but their numbers are not great until the bone marrow is almost completely replaced by Gaucher's cells in the malignant osseous type (see Melamed and Chester's case). The degree of leucocytosis appears to have no relation to the amount of bone destruction. It is probably a nonspecific reaction to splenectomy. Connors reported leucocyte count of 13,000 in one of his patients 17 years after a splenectomy done for traumatic rupture of the spleen.

It has been alleged that splenectomy precipitates or hastens involvement of the bones in Gaucher's disease. This will be difficult to prove until someone has the opportunity to remove the spleen in one of a pair of identical Gaucher's twins. De Lange felt that there was retardation of the skeletal involvement in the splenectomized girl as compared to the sister. Of the patients reviewed in this paper 4 had bone changes before splenectomy, 4 developed bone lesions after splenectomy while 4 others had no evidence of skeletal

involvement in the 7, 11, 13, and 28 year periods following their respective splenectomies. As splenectomy is only done at a time when Gaucher cell infiltration is in a rampant phase, it seems unreasonable to attribute postoperative bone involvement to the mere removal of the spleen.

As a general rule, the earlier in life that the disease gives rise to symptoms, the worse the prognosis, and therefore the earlier the splenectomy, the worse the outlook. Yet Erdmann and Moorhead's case and de Castro Freire's show that one may not be arbitrary in withholding the benefits of splenectomy from young children. In neither of these patients has purpura recurred, nor have bone complications arisen.

As to the ultimate value of splenectomy in Gaucher's disease, the long histories of these patients is encouraging. The bone lesions in the older patients have not progressed to total skeletal involvement except in the fatal case described by Melamed and Chester, while in certain instances there has been evidence of arrest and repair. They are in fair general health and carry on as normal individuals. One of them has raised a family. Their present ages are 33, 36, 44, 48, and 1 was aged 60 in 1929 (Hunter and Evans' case).

Of the 5 children, 2 died before the age of 10 years. The others have arrived at the ages of 12, 19, and 31 years. Of the splenectomized patients who have died, 2 died of the malignant osseous form and 1 of the pulmonary form. None died as a result of intercurrent infection. Although this series of cases, followed for more than 5 years, is small, it is of interest to note that there has been freedom from acute intercurrent infection in the entire group. If splenectomy increases the resistance of the Gaucher patient to acute infections, which is reputed to be the chief cause of death in this group of individuals, the operation would be justified on this ground alone.

#### SUMMARY

1 A short review of Gaucher's disease is given, with the report of a case 7 years after splenectomy.

2 Late reports are made of several cases previously described in the literature, ranging from 5 to 28 years after splenectomy.

3 Similar cases from the world literature are reviewed.

4 The mortality rate for splenectomy in Gaucher's disease is nearer 15 than 20 per cent. Those patients who survive the operation show striking immediate clinical improvement, which is usually maintained, except in very young children.

5 The theory that splenectomy hastens the involvement of bone in Gaucher's disease is questioned.

6 It is suggested that splenectomy increases the resistance of the Gaucher patient to infection.

I wish to express my thanks to Dr. Eugene H. Pool, Dr. John J. Moorhead, Dr. George T. Pack, Dr. Arthur Purdy Stout, and Dr. Allen O. Whipple for their generosity in allowing me to use data on their cases from their private files.

#### BIBLIOGRAPHY

- 1 ABALLI, A. J., and KATO, J. Gaucher's disease in early infancy, a review of literature and report of a case with neurological symptoms. *J. Pediatr.*, 1938, 13, 364-380.
- 2 ANDERSON, J. P. Hereditary Gaucher's disease. *J. Am. M. Ass.*, 1933, 101, 979-981.
- 3 ATKINSON, F. R. B. Gaucher's disease in children. *Brit. J. Child Dis.*, 1938, 35, 1-22.
- 4 CARLING, E. R., CARLILL, H., and PULVERTAFT, R. J. Splenectomy in Gaucher's disease with hemoglobinuria. *Proc. Roy. Soc. Med.*, 1932, 26, 361.
- 5 CONNORS, J. F. Splenectomy for trauma. *Tr. Am. Surg. Ass.*, 1928, 46, 68-83.
- 6 CUSHING, E. H., and STOUT, A. P. Gaucher's disease, with report of a case showing bone disintegration and joint involvement. *Arch. Surg.*, 1926, 12, 539-560.
- 7 DE CASTRO FREIRE, L. De la splénectomie dans la maladie de Gaucher. *Arch. de méd. d'enf.*, 1935, 38, 163-166.
- 8 DE LANGE, C. Ueber Zeitfolge des Entstehens und ueber Heilungstendenz der Skelettveraenderung beim Morbus Gaucher sowie ueber das Erscheinen der typischen Pigmentationen. *Ann. paediat.*, 1938, 152, 87-94.
- 9 DONOVAN, E. J. Splenectomy in child 11 months of age for Gaucher's disease. *Surg. Clin. N. America*, 1931, 11, 517-520.
- 10 EPSTEIN, EMIL. Beitrage zur Chemie der Gaucher'schen Krankheit. *Biochem. Ztschr.*, 1924, 145, 398-414.
- 11 ERDMANN, J. F., and MOORHEAD, J. J. Splenectomy for splenomegaly (Gaucher type). *Am. J. M. Sc.*, 1914, 147, 213-224.
- 12 GAUCHER, E. De l'écithélioma primitif idiopathique de la rate hypertrophie sans leucémie. *Thèse de doct.*, Paris, 1882.
- 13 HOFFMAN, S. J., and MAKLER, M. I. Gaucher's disease, review of literature and report of case diagnosed from section of inguinal lymph gland. *Am. J. Dis. Child.*, 1929, 38, 775-793.
- 14 HORSLEY, J. S., JR., BAKER, J. P., and APPERLY, F. L. Gaucher's disease of late onset, with kidney involvement and huge spleen. *Am. J. M. Sc.*, 1935, 190, 511-518.
- 15 HUNTER, D., and EVANS, W. Gaucher's disease thirteen years after splenectomy. *Proc. Roy. Soc. Med.*, 1929, 23, 224-225.
- 16 MANDELBAUM, I. S. Two cases of Gaucher's disease in adults, a study of the histopathology, biology and chemical findings. *Am. J. M. Sc.*, 1919, 157, 366-389.
- 17 MELAMED, S., and CHESTER, W. Osseous form of Gaucher's disease, report of case. *Arch. Int. Med.*, 1938, 61, 708-807.
- 18 MUELLER, H. Ueber die sogenannten primären Lipoidosen. *Ztschr. f. Kinderh.*, 1938, 59, 476-498.

9. MYERS, B. Gaucher's disease of lungs. Brit. M. J. 937, 8.
10. Idem. Gaucher's disease: splenectomy. Proc. Roy. Soc. Med. 935, 26, 150-56.
11. PACK, G. T. and SILVERSTONE, S. M. Gaucher's disease: report of case improved after splenectomy. Am. J. Surg. 935, 4, 77-86.
12. PINK, L. Classification of diseases of lipid metabolism and Gaucher's disease. Am. J. M. Sc., 935, 85, 453-459.
13. Idem. Die Skelettforn (osteoporose form) des Morbus Gaucher. Jena. Gosta. Flscher. 9, 7.
14. PIRCE and RAMON. Quoted by Erdmann and Moorhead ( ).
15. POOL, E. H. Gaucher spleen. Ann. Surg. 9, 74, 635-57.
16. Idem. Discussion—Surgery of the spleen. T. Am. Surg. Ass. 928, 26.
17. POOL, E. H. and HOWELL, R. W. Effects and results of splenectomy in variety of conditions. Surg. Clin. N. America, 930, 439-440.
18. POOL, E. H. and STELLMANN, R. O. Surgery of the Spleen. P. 30. New York: D. Appleton & Co., 933.
19. POTTER, E. P. and McRAE, C. C. Gaucher's disease: report of 1 case with remission in one following administration of ether extract. Am. J. M. Sc. 935, 85, 92-96.
20. ROWLAND, R. S. and STEWART, R. H. Gaucher's disease. In Practice of Pediatrics (Brennemann), 937, 3, Chap. 3, pp. 6-80.
21. SPACHMAN and MACKIE. Quoted by Abell and Kato ( ).
22. ULLRICH, O. Splenektomiefolgen beim Morbus Gaucher. Ztschr. f. Kinderh., 935, 55, 71.
23. VOYER, F. and BARNES, F. A. Erythrocytic marrow of children in normal and in pathologic states. Am. J. Dis. Child. 932, 37, 245-268.
24. WHEELER, H. F. and GUYARSON, E. Gaucher's disease associated with multiple telangiectases in an elderly woman. N. York State J. Med., 1940, 40, 15.
25. WHITELY, A. O. Studies in splenopathy: Introduction. J. Am. M. Ass., 936, 97, 771-776.

# EDITORIALS

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## WAR MEDICAL SERVICE IN GREAT BRITAIN

THE success of the British fighting forces in opposing the Nazi Colossus has appealed to the imagination and sympathies of the American people to such an extent as to obscure the working of some of the machinery that made such achievements possible. The result alone seemed important and only a few bothered to lift the hood to look at the engine. Among the various essential parts of this mechanism is the medical organization, and it may be of interest to American doctors to learn something of how it is working and what it is accomplishing.

In the first place it is essential to point out that the medical corps of the army and navy are playing but a small part in medical relief work in Great Britain. In defensive preparations prior to the war the planning commissions envisaged the probability of large scale air raids on cities and industrial areas from the outbreak of the war and it was fore-

seen that the care of civilian casualties might be a more important problem for the medical organization than that of military casualties. In addition the civilian population would present other health problems growing out of the evacuation of refugees from the cities and the crowding together in public shelters of those who remained. So in addition to the medical corps of the army and navy and of the separate air force a fourth civilian organization known as the Emergency Medical Service or "E M S" for short was set up under the Minister of Health.

The responsibilities of these four different services are separate but related. The medical corps of the Royal Navy is the most nearly independent service and comes closest to doing what it was intended to do, namely care for the illnesses and casualties among the naval and fleet air arm personnel. It has its hospitals scattered about England and elsewhere, chiefly at the various naval bases. The writer visited one of these hospitals in October. It was situated in a coast city that was very exposed to air bombardment. The buildings were ancient and built in years when sail still provided the motive power of ships. The receiving and operating rooms were well organized in the subterranean vaults and were well organized. Each case was inspected on admission and tagged either to be sent to the resuscitation room, to the operating room via x-ray, or to the ward. Shock teams were organized to work in the resuscitation room and were able to draw on an ample blood bank and stores of plasma or dried serum obtained and prepared by the hospital. A number of severe burn cases were under treatment and apparently this is a not infrequent type of

naval casualty resulting either from fires or bursted steam pipes. It is to be noted that this hospital handled civilian casualties as well as those suffered by naval personnel. Because of its exposed position patients treated there had to be evacuated as soon as they were transportable and they were then sent on to an E. M. S. Hospital farther inland.

The Royal Army Medical Corps maintains only a few general hospitals in England but does have a number of small camp hospitals where medical and minor surgical conditions are handled. A number of general hospitals were established in northern France during the time that the British Expeditionary Force was holding its sector at the front. Here too was assembled the best part of the fine motorized equipment organized for the medical and surgical care of the army in the zone of combat. These included mobile operating units, x-ray vans, laboratory and other cars. All of these were lost in the battles of Belgium and Northern France. The plans of medical organization called for the evacuation of the wounded from the army general hospitals to E. M. S. hospitals in England. These plans were put to a hard test in the evacuation of the wounded from Dunkirk. Most of the wounded had to be rushed from the place where they fell directly on board ship without receiving other than first aid treatment. Often it was several days before they reached their destination in hospitals in England. The difficulty of properly handling the wounded in the confusion of the embarkation and debarkation, with the well and injured hopelessly mixed may be well imagined. Yet somehow the authorities proved equal to the occasion and the wounded were sorted, loaded on hospital trains, and distributed all over England, for the main part to E. M. S. hospitals. Although many of the wounds proved badly infected and gas infection was common it was the gen-

eral impression that the condition of the patients upon arrival was less bad than might have been anticipated. This was generally attributed to the widespread oral administration of sulfanilamide begun at the first aid post and continued throughout the journey. Although there was no opportunity for proper control of the drug by blood level determinations and the dosage had to be regulated according to the judgment of the different doctors who were in charge, still the effect in general was beneficial and undoubtedly played a part in preventing many of the more virulent types of infections.

The Royal Air Force being an independent service, maintains its own separate hospitals for the treatment of its officers and men. Because of the importance from the standpoint of national defense of restoring flying personnel to service as rapidly as possible, special facilities were arranged for the prompt transfer of these men from other hospitals where they might be taken immediately after injury to the special R. A. F. hospitals where a staff of specialists was assembled and all facilities provided to bring about as quick a recovery as possible. Not all patients were transferred however and exception was made when the patients required special treatment which could be best obtained at other hospitals. This was the case with the burned aviators who were treated at special faciomaxillary centers maintained by the Emergency Medical Service under the direction of the distinguished plastic surgeon, Sir Harold Gillies.

Severe burns of the face and hands proved a common type of injury among aviators whose planes were set on fire in aerial combat. During the process of getting out of the cockpit in order to bail out by parachute their faces and hands were exposed to the flames while their bodies were relatively protected by their heavy flying costumes. These men were ter-

ribly disfigured and frequently required complete reconstruction of nose, mouth, and eyelids in addition to skin grafts to the face. Such operations must be done in different stages over a period of many months, but beautiful work is being done and they are being made fit again to return to human society. The burns of the hands also represented a difficult problem requiring co-operative effort from both plastic and orthopedic surgeons to achieve the best results. The study of these cases, the majority of which were treated in the beginning by tanning of the necrotic tissue with various solutions, led to the important conclusion that without prejudice to the use of tanning in other parts of the body, in the case of the face and hands it caused excessive tissue loss and scar formation and should be abandoned. An order to this effect was issued to the R A M C and E M S hospitals.

The Emergency Medical Service in the Ministry of Health is the new organization developed to meet the special conditions that were expected to arise in this war. It is entirely civilian and there is no uniform. It admits to its hospitals for treatment first, any disease or injury arising in or incurred by personnel of the military forces whether army, navy, or air force, second, civilians with injuries incurred as a result of enemy action or in the course of civil defense, and third, civil cases of any character that have to be sent in on account of the necessities of war, as for example the evacuation of a hospital that has been subjected to aerial bombardment.

At the outbreak of the war the E M S constructed or improvised a large number of hospitals throughout England. For the most part these were mental hospitals which were evacuated of their patients and converted to general medical and surgical use, or hut hospitals built usually about a nucleus of pre-existing buildings which supplied power and

service. The administration is regional under hospital officers and group officers. These men are responsible for supplying staff and personnel and also for the transportation and distribution of the convoys of sick and wounded who must be evacuated from regions threatened with aerial bombardment.

The city of London is divided into six or seven sectors shaped like a section of pie each with its apex extending into the central part and including one of the important teaching hospitals such as Guy's, St Bartholomew's, St Mary's, St Thomas', etc., which is supposed to control the whole sector. The sector stretches peripherally for a considerable distance, and its base may be as much as 50 miles distant from its peak. A number of E M S hospitals are included in each sector and theoretically these hospitals are staffed by doctors and nurses from the dominating hospital and medical school at the apex. This is in order that these hospitals may work together with the minimum of friction and that all of them may be utilized in the education of medical students and nurses. The medical staffs of the E M S are all in the employment of the Ministry of Health and for the most part on a full time basis, although some are on half time. The salaries are meager, ranging from 500 pounds for a junior physician or surgeon to 800 pounds for a senior with an additional allowance of 100 pounds for living expenses. It may be remarked in passing that private practice is so completely disrupted in London and many of the other large cities that many of the doctors are completely dependent on these salaries for their living.

Because of the constant threat of air bombardment a large number of the beds in the central hospitals must be kept empty. This is both for the protection of patients and also to provide facilities for the reception of the large numbers of air raid casualties that might



be produced at any moment by an unlucky hit. Most of the important hospitals in London have sustained severe damage from bomb hits and it is estimated that it will be necessary, to replace the entire hospital plant of London at the end of the war. Emergency operating and nursing facilities have been organized in the basements of these hospitals and here are treated the ordinary urgent civilian conditions as well as the air raid casualties. Only small staffs of doctors and nurses are maintained. As quickly as possible the patients are evacuated and transported to the more outlying hospitals in the respective sectors where their security will be greater than in central London and better care can be given.

All of these hospitals are regularly supplied with citrated blood, plasma, and dried serum from one of the four blood depots organized by a committee of the Medical Research Council. In the American section of the Park Prewett Hospital at Basingstoke the blood depot supply truck called regularly every Monday and delivered twelve half liters of blood and took away the unused remainder of the blood that had been left from the previous week, to be converted into plasma. The blood supply service also replenished the stock of plasma and dried serum and kept it up to an

agreed level. This was a fine service and was available to all those hospitals which requested it.

Finally in any comment upon the medical organization in England one must pay tribute to the fine spirit of devotion and sacrifice of the doctors and nurses. These men and women have faced the dangers and miseries of air raids without complaint. Many have been killed or wounded. They have never stinted their services in furnishing medical and nursing care and in times of danger have remained with their patients and tried to provide for their protection. Their spirit has been typical of the English people as a whole and they have faced every trial with a jest. Frequently when I encountered a British medical colleague he would remark quite casually and as if it were a great joke that he had received news that his house in London had been hit by a bomb. Although this generally represented the loss of all that had been collected during a life time none of them wanted sympathy. But if one explored the matter further one might elicit some poignant remark such as "Well it is rather hard on my wife because she is too old to start all over again." One returns to the United States with the feeling that we Americans may take pride in our British heritage.

PHILIP D. WILSON

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

IN the first chapter of *Gynecological and Obstetrical Pathology*<sup>1</sup> the author gives a brief review of the endocrinology of the menstrual cycle and pregnancy, and calls attention to the histological changes produced by the hormones involved

Each subsequent chapter starts with a short description of the normal histology of the particular part to be considered which is in turn followed by a description of the pathological changes. Brevity and conciseness characterize the descriptions throughout the book, however, each phase of pathology is allotted its proper consideration.

The book contains 495 pages and 42 well chosen illustrations. All the illustrations, but one, are in black and white. A bibliography is presented at the end of each chapter. This treatise is a very valuable reference for the student or practitioner of gynecology.

CHESTER C DOHERTY

FOUNDATIONS for further research in neurohistology have been laid in the 164 page monograph of Professor Boeke.<sup>2</sup> The book is divided into four chapters which cover (1) innervation of skin, (2) the sympathetic ground plexus, (3) the relation of sympathetic interstitial cells to neurons and to humoral phenomena, and (4) a critical discussion of the neuron doctrine. The general objective of the work is the correlation of physiologic and histologic observations. In his study of regeneration of nerves to the skin, the author was not able to confirm Head's theory that protopathic sensibility was mediated by nerves of the sympathetic system, but found that such sensibility was a phase associated with regeneration of somatic nerves. Numerous examples are cited to show the widespread distribution of the sympathetic ground-plexus to all parts of the body. Interstitial cells are discussed with reference to their possible functions and the meaning of their presence in higher vertebrates to phylogenetic development as traced from invertebrates through *Amphioxus* and the sharks. The final chapter is devoted to pointing out some of the inadequacies of the neuron doctrine as it exists in its classical form, and a plea is made to regard synapses as living membranes which possess physiologic continuity. The syncytial character of many nerve plexuses is regarded to be out of harmony with the idea of strict discontinuity of individual neurites. The author states frankly that the treatise is colored by his own

opinions, but that much of the material deals with controversial subjects in which it is often better to leave a question open than to draw unwarranted conclusions.

The book is better suited to the needs of the more advanced student in neurohistology or neurophysiology than it is to those of the beginner, because the author presupposes a knowledge of the literature on the part of the reader. It also should be very readable to the clinical neurologist. There are 48 text figures and a bibliography of 88 references. Some figures are taken from older works (as far back as 1894), but most of them are relatively new. The bibliography is representative rather than exhaustive.

HAROLD A DAVENPORT

THE approach to the diagnosis of "the acute abdomen" by Cope<sup>3</sup> is essentially a clinical one. A composite picture that includes the phenomena of pain, tenderness, rigidity, nausea and vomiting, and the localizing phenomena, plus such systemic signs as fever, pulse increase, and leucocytosis, is present with certain variations in all types of the acute picture. Clinical experience and judgment, with a discernment for shadings, enable us to differentiate, for instance, acute appendicitis from acute salpingitis, cholecystitis, or other lesions. This approach and clear appraisal of clinical symptoms is excellently accomplished in this compact volume now in its eighth edition.

The subject matter is contained under the following chapter headings: principles of diagnosis in acute abdominal diseases, methods of diagnosis, appendicitis, perforation of gastroduodenal ulcer, acute pancreatitis, acute abdominal obstruction, intussusception, carcinoma of the colon, strangulated hernia, ectopic gestation, cholecystitis. There are other additional chapters on the colics, abdominal injuries, abdominal disease with genito-urinary symptoms, acute peritonitis, and diseases which simulate an acute abdomen.

The author has wisely made the chapter discussing appendicitis the most extensive, as well as a pivotal point for differential diagnosis. The chapter is undoubtedly the best of the group. There is little room for fundamental difference of opinion with ideas expressed by the author. The clinical picture of each disease is well drawn and excellently written. One minor criticism might be ventured, namely, the presentation of perforated ulcer in clinical "stages."

<sup>1</sup>GYNCOLOGICAL AND OBSTETRICAL PATHOLOGY WITH CLINICAL AND ENDOCRINE RELATIONS. By Emil Novak, A.B., M.D., D.Sc. (Hon. Dublin). F.A.C.S. Philadelphia and London: W. B. Saunders Co. 1940.

<sup>2</sup>PROBLEMS OF NERVOUS ANATOMY. By J. Boeke, LL.D. (Glasg.) 1st ed. London: Oxford University Press, 1940.

<sup>3</sup>OXFORD MEDICAL PUBLICATIONS. THE EARLY DIAGNOSIS OF THE ACUTE ABDOMEN. By Zachary Cope, B.A., M.D., M.S. (Lond.). F.R.C.S. (Eng.) 8th ed. London: Oxford University Press, 1940.

This work is a handy volume. It is accurate, complete and groups acute diseases of the abdomen in one volume.  
J. R. BROOKHOFER.

THE volume *Surgery of the Alimentary Tract* by Devine<sup>1</sup> is a large one as might be surmised from its title. It is divided into four sections: (1) the diagnosis of surgical dyspepsia, (2) the surgery of surgical dyspepsia and of the upper part of the abdomen, (3) abdominal emergencies which may involve either the upper or the lower part of the abdomen and (4) surgery of the lower part of the abdomen.

In the first section the author has made an unusual and instructive approach in thorough discussion of the dyspepsias, both gastroduodenal and retrogastric, or reflex. A thorough and sound explanation of the mechanism and correlated clinical picture is given. A wide section is devoted to ulcer—gastric, duodenal, and jejunal ulcer—duodenal diverticulum, gastritis and duodenitis, and carcinoma.

The second section of part one of the text deals with "precise" methods of diagnosis, chiefly x-ray and includes a chapter on the gastroscope.

Under "surgical procedures" there is an extensive and well illustrated section dealing with the operative surgery of the stomach, duodenum, bile tracts, pancreas, and spleen, as well as a section on post-operative complications. On the operative management of duodenal ulcer the author is less radically inclined than continental surgeons and perhaps less so than most American surgeons. If the "infective" type of ulcer he employs gastro-enterostomy in the "acidic" type partial gastri resection, his feeling being that in the ulcer of his peoples the "infective" type predominates. A considerable amount of space is devoted to the technique of resection for both ulcer and carcinoma and there are tremendous number of excellent illustrations—far more than are usually found in a text on gastroduodenal surgery.

In the fourth section are included appendicitis, carcinoma of the colon and rectum and diverticulitis.

One cannot but be impressed by the obvious experience of the author, as shown by the abundance of careful descriptive detail and illustrations in the preparation, approach, and performance of operations. The work represents a fine contribution to the surgical dyspepsias, and particularly it is an excellent reference volume for the surgeon interested in the surgery of the stomach and duodenum.

J. R. BROOKHOFER.

In the revised edition of Professor Grant's *A Method of Anatomy Descriptive and Deductive* an introductory section on the bodily systems has been added to the text material, and over one hundred

the original set of illustrations—making a present total of 65. Many of the new figures are less diagrammatic and are therefore better representations of dissections than are those of the original edition.

The first section deals, in general terms, with the several bodily systems. Osseous structure is considered microscopically—bones are classified the significance of markings discussed—vascular foramina, elevations, facets, and foramina. Muscles are described on the basis of internal fascicular architecture and the physiological mechanism of contractions is described in simple terms. The vascular system is considered from many standpoints as is the volume of blood contained in the body as to the character of arteriovenous anastomoses as to special nature of alveolar, end-arteries, and cavernous tissue. Many helpful facts are recorded regarding vascular patterns in such special areas as nail bed and lip, cerebrum and spleen, erectile bodies topographically different parts are thus catalogued together on the basis of peculiarity in blood supply. By this means the student is introduced to a rationalizing scheme of study. The nervous, digestive, respiratory, urinary and reproductive systems are similarly treated in this preliminary section.

The regional account is followed, a section being devoted to each of the major subdivisions of the body, namely upper limb, lower limb, pelvis and perineum, thorax, head and neck. A closing section covers the autonomic nervous system, body types, the separate elements of the skeleton.

Throughout these sections the anatomical detail is presented with admirable ingenuity, simple mechanical principles, homely physical notions are abundantly cited in order to make structural facts familiar and, therefore, mentally manageable. Thus, in discussing the musculature the attachments of the upper limb the head is likened to guy ropes the looseness of the pectoral fascia is explained as adaptive to free thoracic movement during respiratory activity marginal thickening of the scapula is said to prevent buckling of that bone when the serratus anterior pulls upon the inferior border the carpal bones are presented as modified blocks, altered from cubical to various other forms.

In the section about the abdomen the inguinal canal is likened to a channel whose roof consists of 3 arcades contributed by the trilateral wall. It is pointed out, strikingly, that the abdominal viscera lie, largely within the thorax cage (because of height of diaphragm) and within the pelvic bowl, the liver is described as resembling an oblong block, the intestines with its mesentery the kidneys with their retroperitoneal stratum are likened to 3 pages of book, comparatively movable after dissection.

In the section dealing with the anatomy of the lower limb complex anatomy is again simplified by comparison with common objects the space of the femoral triangle, with its combination as adductor canal is likened to funnel with a long spout the weight-bearing points of the foot suggest the supportive mechanism of tripod. The chapter con-

<sup>1</sup>THE SURGERY OF THE ALIMENTARY TRACT. By Dr. MARK DEVINE. M.D. PRACTICAL. Baltimore: The Williams & Wilkins Co.

<sup>2</sup>A METHOD OF ANATOMY, DESCRIPTIVE AND DEDUCTIVE. By J. C. GRANT, M.D. CH. 1. C.B. (Edin.) and Baltimore. The Williams & Wilkins Co. 1920.

tains tables of muscle action groups and time tables of epiphyseal development

The section on thoracic anatomy, in addition to dealing with the regular segregated items, discusses such varied general topics as posture, alteration in form of the bronchial tree, development of the heart and great arteries

The section on the anatomy of the head and neck is, like the preceding sections, replete with diagrammatic figures. Some of these are cryptic and would require an experienced student's knowledge for full understanding. Others are better representations of dissections or of gross sections, and are, therefore, distinctly helpful.

Professor Grant's *Method of Anatomy* resembles a manual more closely than it does any other type of treatise, but it differs from the standard manual in presenting concepts superabundantly. It is not a textbook of the regular systematic order, the bulk of its content being arranged upon a regional basis. The volume is not a substitute for an atlas, since the drawings are diagrammatic, it is not a dissector's guide, but is now accompanied by a small companion volume which serves the student in the latter capacity.

This book, which is essentially a manual of regional anatomy filled with concepts, is unique in its attempt to teach anatomy in such a way that underlying principles, rather than mere facts, are made its chief content. Certainly only a gifted teacher could formulate as many valuable notions as Professor Grant has included in his volume. His experience has allowed him to furnish some of the clearest bits of description yet encountered in anatomical writings. But in the commendable desire to clarify and to simplify, some important details of anatomy are omitted, simplification becomes so demanding that what remains of fundamental description is actually quite "traditional."

Professor Grant's provocative volume could scarcely replace any regular part of the student's anatomical library, but it could, with great profit, be added to such a library. For the graduate student its content would be inspiring, the surgical anatomist could profitably employ it as a source book for lecture material, and it would carry the young teacher glowingly through those beginning years which, customarily, are depressingly didactic. BARRY ANSON

THE author of *The Injured Back and Its Treatment*<sup>1</sup> does not claim that the content of this book is new. For those who have kept abreast of modern developments in trauma and diseases of the spine, it is intended as a compilation of modern concepts in this field and as a bibliography in which all important related work is made available. For those whose attitude toward back pain is one of fear and helplessness, a complete and concise course in the anatomy, pathology, physiology, diagnosis, and treatment of any related condition is available. For

the practitioner who for the first time sees the patient with a lesion of the spine or its related structures, the chapter on the routine examination of the back should prove most valuable, for it is the guide by which he may evaluate the patient's complaints, discard the irrelevant, and localize those factors playing a major rôle in the clinical picture. The editor has wisely refrained from accentuating those lesions which are amenable to operative management alone. The prolapsed intervertebral disc and other causes of cord and nerve compression are discussed but with the reserve warranted by their relative infrequency.

This book has been published at an opportune time. It is alone in the field and is a "must" number for the medical library. J K STICK.

NOT only have Lowsley and Kerwin<sup>2</sup> amplified and enlarged their original textbook on urology to a two volume work but they have succeeded in compiling one of the most comprehensive and valuable editions on this subject which has appeared in recent years. While the book is written primarily for the medical student, the general practitioner, and the general surgeon, it also provides a completely up to date reference work for the trained urologist.

General diagnostic procedures, with special emphasis on their practical value, are considered in great detail in the early text. Roentgenography of the genito-urinary tract is adequately considered and well illustrated. This is followed by an excellent chapter on anesthesia in urology. Embryology, anatomy, anomalies, and physiology of each division of the male genito-urinary, and the female urinary, organs are fully described before injuries and diseases are discussed. The most outstanding feature of this work is the very complete consideration of treatment of all urologic diseases and anomalies. The excellence of the illustrations by Didusch clarifies each surgical procedure, making the work an atlas of urologic surgery in addition to the text. A full and complete bibliography is appended to each chapter.

This work can be most heartily recommended, not only as a textbook, but as a suitable reference which covers the entire field of modern urology.

VINCENT J O'CONNOR

IN the latest revision of their book about diseases of infancy and childhood, Drs Holt and McIntosh<sup>3</sup> acknowledge the inability of any one or two authors to write with authority on such a broad specialty as pediatrics. Increasing specialization within the pediatric field has enabled investigators to acquire information and experience which it is impossible for the general pediatrician to obtain.

<sup>2</sup>CLINICAL UROLOGY. By Oswald Swinney Lowsley, A.B. M.D. F.A.C.S. and Thomas Joseph Kirwin, M.A. M.S. M.D. F.A.C.S. Vols. 1 and 2. Baltimore: The Williams & Wilkins Co. 1940.

<sup>3</sup>HOLT'S DISEASES OF INFANCY AND CHILDHOOD. A TEXTBOOK FOR THE USE OF STUDENTS AND PRACTITIONERS. By the late L. Emmett Holt, M.D. and John Howland, M.D. Revised by L. Emmett Holt, Jr. M.D. and Rustin McIntosh, M.D. 11th ed. New York and London: D. Appleton Century Co. 1940.

<sup>1</sup>THE INJURED BACK AND ITS TREATMENT. Edited by John D. Ellis, M.D. Springfield Ill. and Baltimore Md. Charles C. Thomas 1940.

On this account the writers have enlisted the aid of some thirty of their colleagues who have collaborated in certain features of the work. By this means the authors have been able to maintain uniformity of style and presentation, and at the same time to take advantage of the special studies of workers in some particular branch of pediatrics.

The result is a textbook which presents in admirable fashion the essentials of present day pediatric knowledge. Several sections of the book have been entirely rewritten, and others extensively revised and enlarged to bring the subject matter up to date.

This book can be heartily recommended both to students and practitioners. STANLEY GIBSON.

THE volume *Physiology of the Fetus* by Windle, comprising a modest 226 pages, is packed with well indexed and tabulated information bearing strictly on the title. It covers in considerable detail such matters as the function of the fetal circulation, blood, respiration, digestion, elimination, excretion, the neuromuscular system, and sensation.

The obvious difficulties entailed in the investigation of such fetal functions limit the subject matter to a great extent. Yet it was astonishing to one not

intimately associated with such research, to find how much practical knowledge is actually at hand. The author has gathered together his material in a concise and logical manner, has added to it his own considerable number of observations, and has discussed controversial points in a constrained and enlightening manner. At the same time the book makes interesting reading and is not sifted. It is a timely subject which together with similar work on fetal pathology, should speed the time when we shall consider a diagnosis of death from prematurity entirely inadequate. More information of this sort should help the pediatricist to understand better and to treat more successfully many common problems of the newly born, such as asphyxia and cyanotic attacks.

In one respect, however, the reviewer found himself unsatisfied. At the end of each chapter he felt a great curiosity to know just what D. Windle thought about the practical implications of his research. This feeling is mentioned not at all in criticism, but in the hope that future editions may be enriched by his seasoned judgment on the many questions which come to mind. This sort of correlation between research and clinical needs is nowhere more essential than in the care of the premature and newly born infant. This volume should be "must" reading for pediatricists as well as for students and investigators in the field.

C. AUGUSTUS ALDRICH.

*PHYSIOLOGY OF THE FETUS, ORIGIN AND EFFECT OF FUNCTION IN PRENATAL LIFE.* By William Frederick Windle. Philadelphia and London: Saunders Co. 1924.

## CORRESPONDENCE

### RADICAL CURE OF HYDROCELE BY EXCISION OF SEROUS LAYER OF SAC

THE Editor: In the issue of SURGERY GYNECOLOGY AND OBSTETRICS for April, 1920, a new operation for the radical cure of hydrocele by excision of the serous layer of the sac is described by Hugh Young, of Baltimore.

I have been doing this operation in Madras and now in Delhi for about six years. It is the routine

radical operation which I have practised and taught to my students for that time. I am sure Dr. Young

will be interested to know this and at the same time excuse the liberty which I take in pointing it out. I do so in no critical spirit remembering that hemorrhage probably drove me to get down to the serous layer.

M. M. CHAKRAVARTY.

Delhi, India

Lt. Col., Indian Medical Service

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### OBSERVATIONS ON THE PATHOLOGY OF EXPERIMENTAL TRAUMATIC SHOCK

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**A**n essential feature of the shock syndrome is a disparity between the amount of circulating blood and the size of the vascular bed (1, 5, 14, 17). In traumatic shock, this disparity is the result of a marked reduction of the blood volume as a result of a loss of fluid from the circulation into the tissues. However, except in instances of frank hemorrhage, there is still considerable disagreement as to the actual site of this loss of fluid. Some investigators maintain that it is largely confined to the site of injury whereas others hold that, as a consequence of generalized capillary injury, there is a stasis of fluid and loss of plasma throughout the body, particularly marked in the splanchnic area. In the present study an attempt is made to throw further light on this problem by correlating more closely the physiological with the pathological changes in traumatic shock.

In keeping with the concept of generalized capillary injury as a principal factor in the shock syndrome are the extensive studies of Moon and his associates on the pathological changes in shock (11-14). These investigators find as an invariable accompaniment of shock,

regardless of cause, "marked diffuse congestion of the capillaries and venules in visceral areas, especially the lungs, liver, kidneys, and the serous and mucous surfaces, edema, effusions into serous cavities and capillary hemorrhages" (12). The pathological changes are interpreted as evidence that the marked reduction of the blood volume is due to a loss of plasma and stasis of fluid throughout the viscera, particularly in the lungs, liver, and gastro-intestinal tract. Moon's investigations have done much to revive the theory of a traumatic toxemia in shock and are considered to be evidence against the idea of Blalock and others that in traumatic shock loss of fluid at the site of injury is a principal factor in the reduction of the blood volume (2, 3, 4, 9, 10, 15, 16).

Although Moon's observations clearly demonstrated that certain pathological changes may accompany shock, the causal relationship between these changes and the reduction of the blood volume was not shown. It seemed possible that in traumatic shock the primary mechanism was a loss of fluid, not blood, at the site of injury with an initial reduction of the blood volume, and that the generalized capillary change was a phenomenon secondary to the reduction of the blood volume. To determine this point, traumatic shock was

From the Laboratory for Surgical Research, Harvard Medical School and the Surgical and Medical Services of the Peter Bent Brigham Hospital

TABLE I

Experi- ment	Hours after injury	Wt. kg.	Total blood volume	Plasma volume	Hemat- ocrit	Pulse	Respira- tion	Blood pressure	Pathological findings
<b>Thermal Trauma</b>									
1	Control	14	21.20 106	100 52.6	43.8 47	70 144	20 18	57 66	Green examination: There is extensive edema extending to the site of injury. The dependent part of the lungs were purple-red color and appeared gelatinous and friable. There were hemorrhages throughout the viscera. Microscopically there is evidence of generalized secondary injury to the liver, kidney, adrenal, and gastro-intestinal tract.
6	Control	18	21.2 11.6	100 49.6	40 36	148 156	18 16	56 56	Essentially as in Exp.
	Control	27	17.0 77.0	100 51.3	36 64.3	7 67	7 14	51 50	Essentially the same macroscopic changes.
8	Control	24	17.70 88.0	100 47	3.0 36	70 54		1.00 70	Essentially the same macroscopic changes.
	Control	27	1.00 50	100 70	37 57	107 60	20 24	70 70	Animal sacrificed 9 hours after injury. Pathological examination showed marked loss of fluid at site of my and moderate amount of generalized capillary
10	Control	27	27.00 135.0	100 50	36 36	70 70		70 70	Time to be surgically severe injury. The animal died the end of 4 hours. Pathological examination show extensive local loss of fluid, but generalized changes were less marked than in the longer experiments.
	Control	3	60.0 30.0	70 35	46 36	50 1.0	16 18	70 70	Early stages of shock. Green examination showed 4 variations from the normal (Fig. 4). Microscopic changes suggestive to suggest for reaction of the viscera. See text for details.
	Control	25	50.0 25.0	60.0 30.0	36 37	1.00 100	16 12	70 70	Early stages of shock. Pathological examination showed no striking variations from normal. See text details.
	Control	26	—	—	—	1.00 100	20 20	70 70	Early stages of shock. Pathological examination showed no striking variations from the normal.
<b>Mechanical Trauma</b>									
17	Control	26	11.0 18.0	100.0 50.0	43 47	140 156	14 16	70 100	Early stages of shock, following mechanical trauma. Pathological examination shows no striking variation from the normal (Fig. 5).
18	Control	24	16.0 8.0	70 35	33 66	70 61		70 100	Early shock. This dog was more affected by the anesthetic than usual. Note the bloody sputum. Pathological examination disclosed slightly more evidence of generalized capillary injury than usual. T spleen had not been removed.
	Control	25	—	—	33 66	70 70	20 20	70 70	Pathological changes show evidence of generalized capillary injury. But no marked as that seen following thermal trauma.

produced in animals and complete pathological examination of the viscera was made in different animals at varying intervals during the development of the shock syndrome as evidenced by determination of the blood volume plasma volume hematocrit and blood pressure.

#### EXPERIMENTAL PROCEDURE

The experimental procedure was as follows: Large mongrel dogs weighing between 18 and 28 kilograms, were used in all the experi-

ments. Shock was induced either by severe burns or by trauma to the left hind limb. Animals were allowed water but no food for 3 hours before the experiment. Anesthesia was induced by the intravenous injection of sodium pentobarbital in doses of 32 milligram per kilogram of body weight and maintained by small supplementary injections throughout the experimental period. Determinations of the blood pressure pulse respiration, hematocrit, plasma, and total blood volumes were made before and at varying intervals after the

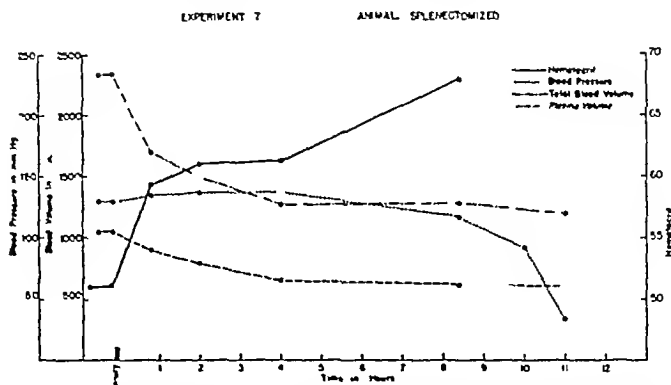


Fig 1 The course of the changes in hematocrit, blood pressure, plasma and total blood volumes in an animal following severe thermal trauma

injury The plasma and blood volumes were determined by the direct method of Gibson and Evans The blood pressure was recorded on a Harvard kymograph by means of a cannula in the right femoral artery Three animals were subjected to mechanical trauma to the left hind limb, administered with a heavy padded hammer in such a manner as to avoid fracturing bones or rupturing large blood vessels Nine animals were subjected to thermal trauma by means of a Bunsen burner applied for periods of 5 to 20 minutes to shaven areas over the thorax and abdomen, constituting approximately one-third of the surface area of the animal's body As soon as the experiment was terminated, a complete postmortem examination was performed and sections of the thoracic and abdominal viscera were taken for microscopic study From all but 3 of the animals (Exp 12, 17, 18) the spleen was removed several weeks before the experiment This was done because previous observations indicated that shock could be produced more readily and more uniformly in the splenectomized dog (10)

Since the changes in the hematocrit, blood pressure, plasma, and total blood volume were quite uniform (Table I), one of the experiments is illustrative (Fig 1) It will be noted that within a few hours of the injury there is marked hemoconcentration Although the plasma blood volume is reduced to nearly two-thirds of its original total, the blood pressure is maintained well above so called "shock

levels" At this early stage of shock, when the blood volume was markedly reduced but the blood pressure was well maintained, the experiment was terminated in 5 instances (Exp 11, 12, 16, 17, 18) by the injection of a lethal dose of the anesthetic The course of an experiment which was so terminated is shown in Figure 2 This animal was subjected to repeated trauma to the left hind limb The rise in the hematocrit is an indication of shock rather than hemorrhage The details of one experiment in which the animal was sacrificed in the early stages of shock are shown in Table II

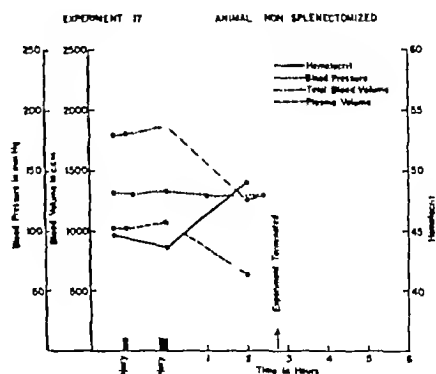


Fig 2 The course of the changes in hematocrit, blood pressure, plasma, and total blood volume following mechanical trauma to the left hind limb The experiment was terminated by a lethal dose of the anesthetic The viscera of this animal are shown in Figure 5



TABLE II.—ANIMAL SACRIFICED IN EARLY STAGES OF SHOCK—PROTOCOL ANIMAL N 160-30  
EXPERIMENT 7 WEIGHT 30.6 KILOGRAMS.

Time	Blood pressure	Pulse	Respiration	Total blood volume	Plasma volume	Heart size	Remarks
8:30 AM							Sodium pentobarbital 0.5 gm injected intravenously
9:30 AM	20	120	14				Cannula in right femoral artery
10:00 AM	28	60	14	1350 cm	1000 cm		
10:30 AM							Animal held. Sodium pentobarbital 1 cm intravenously
10:30 AM	28	160					
10:33 AM							Trocans to left hand knob
10:55 AM		170	13				
11:00 AM							Trocans repeated
11:00 AM	100	180	10				
11:00 AM				1350 cm	950 cm		
11:00 AM	24	170					
11:00 AM							Trocans repeated for respiration
11:00 AM	100	160	10				
11:00 PM	20	200	6				
11:00 PM	20	80	15				
11:00 PM				1300 cm	925 cm		
11:15 PM							Animal sacrificed, 30 cc sodium pentobarbital

Physiological observations. There is cyanosis, swelling, edema and hemorrhage into the tissues of the left leg. The tension of the abdominal wall appears normal. The peritoneal cavity contains no fluid, but the serous surfaces are moist. The mesenteric tract is pale and contracted. The lungs are pink and well perfused. The heart is small and contracted. It contains a moderate amount of blood. No abnormalities are noted in the gross examination of the abdominal viscera (Fig 5). Microscopically no evidence of generalized capillary damage is noted.

#### THE PATHOLOGY OF EARLY SHOCK

Autopsy of animals sacrificed in the early stages of shock revealed marked loss of plasma and fluid at the site of injury but little or no evidence of generalized capillary injury or loss of fluid in the visceral area (Figs 3, 4, 5). Gross inspection of the viscera showed no significant variation from the normal. There was no free fluid in the pleural or peritoneal cavities and the serous surfaces were dry. The heart appeared normal grossly and contained a moderate amount of blood. The lungs were a light pinkish yellow and were dry and crepitant throughout. The liver and kidneys showed no gross variation from the normal. The spleen in the 3 animals in which it had not been removed prior to the experiment, was contracted and firm. The cut surface was dry and little pulp could be scraped off with a knife. The gastro-intestinal tract was often pale contracted and ischemic in appearance (Fig 4). There was no increase present in the weight of the lungs, the liver or the kidneys.

Histologically these observations were substantiated. In the lung (Fig 6) there was no edema, extravasation of red blood cells or leukocytes, or marked engorgement of the alveolar capillaries. In scattered areas there was slight dilatation of capillaries and occasionally polymorphonuclear leucocytic infiltration of the interstitial tissue was found a change which was quite marked in the late stages of shock. The liver showed no significant variation from normal (Fig 7). There was no engorgement of the sinusoids, necrosis of the cord cells, capillary hemorrhage or edema. A moderate number of the cord cells contained fat droplets. The gastro-intestinal tract was singularly free from edema, congestion, submucosal hemorrhages, or engorgement of the serosal vessels. There was no gross or microscopic congestion of the mesentery. The mucosa of the gastro-intestinal tract was well preserved (Fig 8). Thus, in the initial stage of shock the changes in the viscera were more suggestive of hemorrhage than of what has been described as being typical of shock. The



Fig 3 Photograph of the viscera of an animal 4 hours after thermal trauma. The lungs were prevented from collapsing by clamping off the trachea before opening the chest. There is no visceral congestion or effusion of fluid into serous cavities. The omentum is bloodless, and small bowel is pale and contracted. The spleen had been removed.



Fig 4 Photograph of the viscera of an animal 5 hours after thermal trauma. Note that after the chest has been opened the lungs are completely collapsed against the chest wall. There is no congestion or edema of the lungs present nor is there any effusion into the pleural cavities (Exp 12).

kidney was an exception. Although the extreme degrees of congestion described by Moon were not observed, there was slight hyperemia and congestion of the glomerular capillaries even in the early stages of shock. This was particularly striking after thermal trauma, a finding which was in keeping with the fact that gross hematuria was commonly observed within a short time of the injury.

The adrenals showed no striking variation from the normal on gross examination, but microscopically there was hyperemia of the capillaries and an infiltration of polymorphonuclear leucocytes in the zona fasciculata. These changes were not marked but were present in all the dogs of the series. They developed before there was evidence of generalized capillary congestion and engorgement of ves-

sels throughout the viscera. In fact, at this stage the adjacent zona glomerulosa, zona reticularis, and medulla of the adrenal appeared quite normal despite the pathological changes in the zona fasciculata. In a previous study it was shown that these changes develop in the transplanted adrenal gland and hence are not of neurogenic origin (7).

The slight hyperemia of the pulmonary capillaries, the occasional infiltration of the interstitial tissue of the lung with polymorphonuclear leucocytes, the renal and the adrenal changes are interpreted as evidence that, under the conditions of our experiments, there are slight systemic tissue changes in early shock. The possible relation of these changes to the use of sodium pentobarbital as the anesthetic will be discussed later. However, re-



Fig. 5 Photograph of the viscera of an animal 4 hours after trauma to the left hind limb. The gross appearance of the viscera is not unlike that seen following hemorrhage. That this animal, as in shock, is shown by the rise in hematocrit (Fig. 5).

Regardless of cause these pathological changes are not sufficient to account for the marked reduction of the blood volume. Moreover as will be shown later they can be produced without a reduction of the blood volume. It is significant, therefore, that at this early stage of shock there was extensive swelling, edema, and extravasation of fluid at the site of injury. Furthermore, previous observations indicated that the calculated gain in fluid content of the injured area closely approximated the reduction of the blood volume (10). It is concluded that under the conditions of these experiments the principal loss of fluid in the early stages of traumatic shock is at the site of injury.

#### THE PATHOLOGY OF LATE SHOCK

In the experiments (Nos. 5, 6, 7, 8, 9, 10, 19) in which the animals were allowed to survive

for longer periods of time—6 to 12 hours—or until death occurred a somewhat different pathological picture was found. It is important to emphasize that inasmuch as shock depends upon the reaction of different animals to a variety of stimuli, standardization of experimental shock is difficult, and therefore the time factor in these experiments is not an absolute one. Certain animals develop the pathological changes of late shock in a shorter time than others. In general however the longer the animals survived the more striking were the generalized tissue changes. The extreme degrees of generalized capillary injury, visceral congestion and effusion into serous cavities described by Moon were not found in any of these experiments. However microscopically there was a definite change in that direction and in less acute experiments which permitted the animals to survive for longer periods of time the changes might become more marked. The details of one experiment in which the animal was sacrificed in the later stages of shock are presented herein in Table III.



Fig. 6 Photomicrograph of the lungs of the same animal as in Figure 5. There is no edema or extravasation of red cells or engorgement of the alveolar capillaries. Hematoxylin-eosin stain. X 200.

Gross examination of the viscera in the late stages of shock, after compensation had failed and the blood pressure had fallen, showed patchy areas of purplish discoloration in the lungs, particularly in the lower lobes. Microscopically (Fig 9) there was engorgement of the alveolar capillaries, extravasation of cells and fluid into the alveolar spaces, and infiltration of the interstitial tissues with polymorphonuclear leucocytes. No micro-organisms were demonstrated. In the gastro-intestinal tract there were varying degrees of hyperemia, submucosal hemorrhages, and occasionally ulcerations in the duodenum or jejunum. The mucosa was frequently poorly preserved and the small vessels of the bowel were markedly congested (Fig 10, 11). The liver was deep purplish red, and the cut surface was soft and friable. Fluid and blood oozed from it when it was sectioned. On microscopic examination there was found dilatation and engorgement of capillaries, congestion of the sinusoids with red blood cells, and degenerative changes in the cord cells (Fig 12). The kidneys appeared normal in size. On section, the demarcation of cortex and medulla was present, but the organ was deep purple, and a considerable amount of

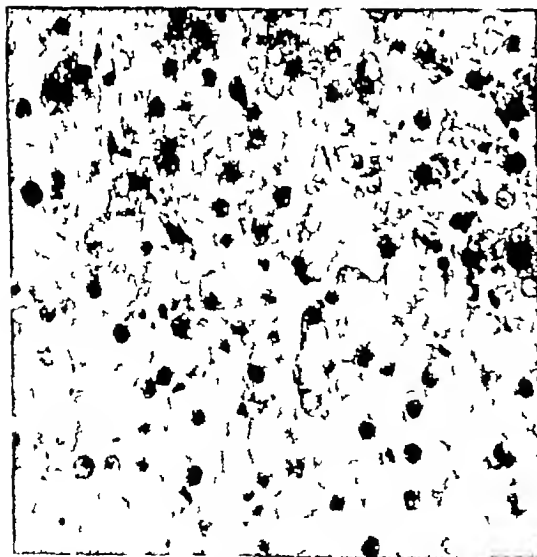


Fig 7 Photomicrograph of the liver of an animal 4 hours after thermal trauma. There is a moderate number of fat droplets in the cord cells. There is no striking variation from the normal. Hemotoxylin-eosin stain  $\times 425$



Fig 8 Photomicrograph of the jejunum of an animal 4 hours after thermal trauma. The epithelium is well preserved. There is no congestion, edema, or capillary hyperemia. Hemotoxylin-eosin stain  $\times 425$

blood oozed from the cut surface. Microscopically, there was marked congestion of the glomerular capillaries, degenerative changes in the tubules, and extravasation of cells and engorgement of capillaries in the medulla.

The adrenals were pale white, but on section the cortex showed a reddish colored radial streaking as a result of hemorrhages. Microscopically there was swelling of the cortical cells in the zona fasciculata and a heavy infiltration of polymorphonuclear leucocytes. These changes were most marked in the zona fasciculata but to a lesser extent involved the zona reticularis and, in a few instances, the zona glomerulosa. There was also congestion and dilatation of the small vessels in both the cortex and medulla with occasional areas of hemorrhage. The significance of these changes



Fig. 5. Photograph of the viscera of an animal 4 hours after trauma to the left hind limb. The gross appearance of the viscera is not unlike that seen following hemorrhage. That this animal, as in shock, is shown by the rise in hematocrit (Fig. 6).

Regardless of cause, these pathological changes are not sufficient to account for the marked reduction of the blood volume. Moreover, as will be shown later, they can be produced without a reduction of the blood volume. It is significant, therefore, that at this early stage of shock there was extensive swelling, edema, and extravasation of fluid at the site of injury. Furthermore, previous observations indicated that the calculated gain in fluid content of the injured area closely approximated the reduction of the blood volume (10). It is concluded that under the conditions of these experiments the principal loss of fluid in the early stages of traumatic shock is at the site of injury.

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Fig. 6. Photomicrograph of the lungs of the same animal as in Figure 5. There is no edema or extravasation of red cells or engorgement of the alveolar capillaries. Hematoxylin-eosin stain.  $\times 500$ .

TABLE III—PROTOCOL ANIMAL No 204-38 EXPERIMENT 9 WEIGHT 22.5 KILOGRAMS

Time	Blood pressure	Pulse	Respirations	Total blood volume	Plasma volume	Hematocrit	Remarks
7:40 a.m.	160	160	9				Sodium pentobarbital 25 c.cm. injected intravenously. Abdomen, chest, and flanks shaved. Cannula inserted in right femoral artery. Catheter inserted in bladder. Left jugular vein exposed to facilitate taking samples of blood.
8:50 a.m.	150	164	8	1900 c.cm.	1090	47	
9:15 a.m.							Cannula washed out.
9:21 a.m.							Thermal trauma to both sides of body for 10 minutes.
9:32 a.m.	145	164	10				Sodium pentobarbital 3 c.cm. at 10:07 a.m.
10:15 a.m.	160						Washed out cannula.
10:25 a.m.	160	198	20				
11:10 a.m.	160	180	20				Washed out cannula.
12:00 a.m.							30 c.cm. dark, bloody urine aspirated from bladder.
1:07 p.m.	160	200	20	1600 c.cm.	900	57	
2:36 p.m.	150	210	20				
3:18 p.m.	150	200	20				
3:30 p.m.							Washed out cannula.
4:15 p.m.	130	210	26	1445 c.cm.	675	57	
6:15 p.m.							Animal sacrificed by intravenous injection of 10 c.cm. of sodium pentobarbital.

Pathological examination disclosed extensive loss of fluid at the site of injury. Gross examination of the viscera showed no striking evidence of generalized capillary injury but on microscopic examination the changes described in detail in the text were evident.

#### PENTOBARBITAL SODIUM ANESTHESIA AND THE PATHOLOGICAL CHANGES IN SHOCK

It may be argued that sodium pentobarbital is shock producing and that the reduction of the blood volume and the pathological changes encountered in these experiments are the result of using this agent as an anesthetic. There is no doubt that repeated and prolonged use of the barbiturates produces capillary damage (12). The fact that this agent was used as the anesthetic and that in the early stages of shock little or no evidence of generalized capillary injury was found strengthens our contention that the initial reduction of the blood volume is due principally to a loss of fluid at the site of injury. In the late stages of shock the use of sodium pentobarbital probably plays a rôle in the development of generalized capillary injury, and the degree of shock is probably more severe than would be encountered from the injury alone.

However, control experiments have shown that the anesthetic is not the principal factor in the production of either the pathological changes or the lowered blood volume. Four dogs were subjected to sodium pentobarbital

anesthesia alone for periods of 4 to 16 hours. The physiological changes produced by this agent in a period of 7 hours are shown in Figure 13. Note that there is slight hemoconcentration and an increase in the total blood volume, but the plasma volume remains remarkably constant throughout the experimental period. The increase in the red cell volume is probably due to contraction of the spleen (10). Pathological examination of animals subjected to the anesthetic alone disclosed, in the early stages, that is, within 3 to 4 hours, comparatively little variation from the normal. There was moderate congestion of small and medium sized arteries and veins, and the intestines in two of the experiments had a somewhat dusky hue. The appearance of the bowel contrasted markedly with that seen following trauma. On microscopic examination there was found slight dilatation of vessels in the lungs, kidneys, and adrenals, and in the last mentioned a light infiltration of the zona reticularis with polymorphonuclear leucocytes. This was much less than that seen in the early stage of shock. In other words, the combination of the anesthetic and trauma



Fig. 9. Photomicrograph of the lung of an animal 1 hour after severe burn. There is marked congestion of the alveolar capillaries and extravasation of cells and fluid into the alveolar spaces. Hematoxylin-eosin stain.  $\times 200$ .

in the adrenal gland is not clear and their relationship to the shock syndrome is not established. As will be described later, such changes can be produced by the anesthesia alone with out a significant reduction of the blood volume.



Fig. 10. Photomicrograph of the stomach of an animal 12 hours after thermal trauma showing extensive engorgement of capillaries and small vessels with red blood cells. Hematoxylin-eosin stain.  $\times 3$ .



Fig. 11. Photomicrograph of specimen of tissue removed from the jejunum of an animal 1 hour after the administration of thermal trauma. There is present marked engorgement of the small blood vessels and capillaries. Hematoxylin-eosin stain.  $\times 425$ .

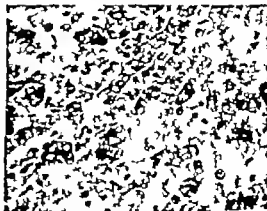


Fig. 12. Photomicrograph of liver of an animal 1 hour after thermal trauma. There are degenerative changes in the cord cells and engorgement of the sinusoids with fluid and red blood cells. Hematoxylin-eosin stain.  $\times 350$ .

than are red blood cells. This would seem to be the principal factor in initiating the reduction of the blood volume and the hemoconcentration. In the late stages of traumatic shock, either as a consequence of prolonged ischemia, adrenal insufficiency, the absorption of hypothetical toxins or factors not yet considered, there develops generalized capillary injury and loss of fluid throughout the viscera, particularly marked in the lungs, liver, kidneys, and gastro-intestinal tract. Thus, the final pathological picture is quite similar to that seen following poisoning, infection, anaphylactic shock, and other states in which capillary injury occurs.

If the late changes of traumatic shock are due solely to ischemia as a compensatory reaction to the reduced blood volume, it should be possible to prevent them by maintaining the blood volume at normal limits throughout the experimental period. This has been accomplished in a study of replacement therapy in experimental shock. The results will be reported in detail in a later publication (6). It can be briefly stated here, however, that plasma appears to be the most effective form of fluid replacement in traumatic shock, not only in restoring the blood volume to normal but also in ameliorating the late pathological changes of shock.

#### SUMMARY

Under the conditions of these experiments in which shock has been produced by thermal and mechanical trauma the principal factor in initiating the reduction of the blood volume is, as Blalock has long maintained, a loss of fluid at the site of injury. In late traumatic shock there is pathological evidence of generalized capillary injury and loss of fluid throughout

the viscera. This appears to be a secondary rather than a primary phenomenon.

The authors are indebted to Dr. Orville Bailey, department of pathology, Harvard Medical School, for the photomicrographs.

#### BIBLIOGRAPHY

1. ATCHLEY, D. W. Dehydration and medical shock. *Med Clin N America*, 1934, 17, 1379.
2. BLALOCK, ALFRED. Experimental shock, cause of low blood pressure produced by muscle injury. *Arch Surg*, 1930, 20, 959.
3. Idem. Trauma to intestines, importance of local loss of fluid in production of low blood pressure. *Arch Surg*, 1931, 22, 314.
4. BROOKS, BARNEY, and BLALOCK, ALFRED. Shock with particular reference to that due to hemorrhage and trauma to muscles. *Ann Surg*, 1934, 100, 728.
5. CANNON, WALTER. *Traumatic Shock*. New York, London: D. Appleton Century Co., 1923.
6. DUNPHY, J. E., and GIBSON, JOHN G., II. The effects of replacement therapy in experimental traumatic shock. (To be published.)
7. DUNPHY, J. E., and KEELEY, J. L. Experimental studies in transplantation of the adrenal gland. *Surgery*, 1940, 8, 105.
8. GIBSON, J. G., II, and EVANS, W. H., JR. Clinical studies of blood volume, clinical application of method employing azo dye "Evans blue" and spectrophotometer. *J Clin Invest*, 1937, 16, 301.
9. HARKINS, H. N., and HARMON, P. H. Plasma exudation, loss of plasma like fluid in various conditions resembling surgical shock, experimental study. *Ann Surg*, 1937, 106, 1070.
10. KEELEY, J. L., GIBSON, J. G., II, and PIJOAN, M. Effect of thermal trauma on blood volume, serum protein, and certain blood electrolytes, experimental study of effect of burns. *Surgery*, 1930, 5, 872.
11. MOON, V. H. Shock, its mechanism and pathology. *Arch Path*, 1937, 24, 642 and 794.
12. Idem. *Shock and Related Capillary Phenomena*. New York: Oxford University Press, 1938.
13. Idem. Circulatory failure. *J Am M Ass*, 1940, 114, 1312.
14. MOON, V. H., and KENNEDY, P. J. Pathology of shock. *Arch Path*, 1932, 14, 360.
15. PARSONS, E., and PHEMISTER, D. B. Hemorrhage and shock in traumatized limbs, experimental study. *Surg, Gynec & Obst*, 1930, 51, 196.
16. ROOME, N. W., KEITH, W. S., and PHEMISTER, D. B. Experimental shock, effect of bleeding after reduction of blood pressure by various methods. *Surg, Gynec & Obst*, 1933, 56, 161.
17. WEISS, S. Syncope, collapse and shock. *Proc Inst. Med Chicago*, 1940, 13, 2.



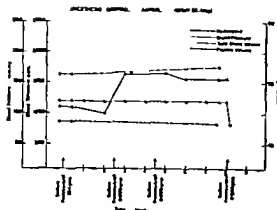


Fig. 3. The course of the changes in the hematocrit, blood pressure, plasma, and total blood volume following the administration of sodium pentobarbital—3 mgm. per kg. of body weight. There is hemoconcentration in keeping with the increase in the total blood volume but no reduction of the plasma volume. The increase in the red cell volume is due to contraction of the spleen.

produced more striking changes in the adrenal than was observed after the anesthetic alone. The gastro-intestinal tract and liver showed no variation from the normal. After longer administration of the sodium pentobarbital 8 to 10 hours, the changes in the lungs, kidneys and adrenals were more striking but there was still no evidence of generalized capillary injury in the other viscera. With large doses over a sufficiently long period of time the late changes of shock can be produced by the barbiturates as well as by a variety of other toxic agents (12).

It is concluded that under the conditions of these experiments the use of sodium pentobarbital as the anesthetic plays no significant role in the early and marked reduction of the blood volume that the anesthetic alone is capable of producing pathological changes in the adrenals, lungs and kidneys similar to those described but that these changes are less marked than those observed when the anesthetic is followed by mechanical or thermal trauma that the changes in the gastro-intestinal tract are not attributable to the anesthetic in the doses used as they were not observed in the control experiments and finally that since it is a toxic agent and known to cause capillary damage the administration of sodium pentobarbital probably accentuates the late patho-

logical changes which have been observed in these experiments.

However the use of sodium pentobarbital does not alter the principal contention of this study namely that in the early stages of traumatic shock there is comparatively little evidence of generalized capillary injury whereas there is obvious and marked loss of fluid at the site of injury.

#### EVALUATION OF STUDY

Although it is generally accepted that a reduction of the effective blood volume is a constant finding in shock, the physiological and pathological mechanisms by which this is brought about are dependent largely upon the causative factors, and hence may differ widely. Shock may thus be regarded as the end result of a variety of pathological and physiological processes. Thus in anaphylactic shock, certain forms of poisoning, infection, and histamine intoxication it is likely that the primary mechanism is generalized capillary injury. This not only increases the size of the vascular bed, thus bringing about a relative reduction of the effective blood volume but eventually as a consequence of loss of fluid and plasma throughout the viscera, produces an actual reduction of the blood volume with hemoconcentration. Histological studies in this form of shock reveal evidence of loss of fluid and cells throughout the viscera (12). On the other hand, in shock due to hemorrhage the primary mechanism is a loss of whole blood from the circulation. There is a compensatory vasoconstriction. Postmortem examination discloses only generalized ischemia of the viscera. If death is not immediate, however and the animal is kept in a state of shock by repeated small hemorrhages, eventually as Blalock (4) has shown, there is evidence of generalized capillary injury and loss of fluids in the viscera. This generalized capillary injury may be the result of prolonged vasoconstriction with consequent ischemia of the viscera.

The present study indicates that in traumatic shock the early physiological and pathological mechanisms are similar to those in shock resulting from hemorrhage except that fluid and plasma are lost in higher proportion

TABLE I—WATER BALANCE DATA AND MCCLURE ALDRICH TEST FOR SUBJECT J N

Date 1935	Body weight gm	Total available water intake gm	Total water output gm	Water balance gm	Hematocrit Per cent	Blood specific gravity	McClure Aldrich test min	
							Arm	Leg
Final 2 days of preliminary period Feb 24	71373	2780	2406	+374	47.96	1.0575	63	68
Feb 25	71378	2526	2536	-10	48.50	1.0598	58	65
Dehydration period Feb 6	71728	688	1853	-1165	48.81	1.0601	58	70
Feb 27	70585	625	1685	-1060	50.14	1.0623	75	61
Feb 28	69588	641	1845	-1204	50.81	1.0631	96	84
Mar 1	68393	1155	1779	-624	50.62	1.0652	66	114
				(Total negative water balance for 4 days 4053)				
Recovery period Mar 2	67802	6917	2404	+4513	49.31	1.0604	62	95
Mar 3	72244	2499	3256	-757	47.18	1.0603	80	96
Mar 4	71355	3327	2931	+396	48.91	1.0619	105	119

pyloric obstruction due to gastric carcinoma. For 2 weeks previous to his admission there had been some vomiting and roentgen-ray examination showed a fair degree of pyloric obstruction. Clinically he showed signs of mild dehydration and loss of weight. In this case the test showed a shortened disappearance time with the mild dehydration and an increase toward normal as fluids were provided. This is precisely the finding one would expect if the test was a good indicator of the state of hydration, as suggested by Hopps and Chris-

topher. However, this was not found to be a constant feature in any of the other cases examined.

Table V shows the data for patient C B who had a cholecystectomy and choledochostomy for a common duct stone with obstructive jaundice. Her postoperative course was essentially uneventful, the jaundice cleared completely and her general condition was good at the time the test was started on January 4, the nineteenth postoperative day. This patient was allowed to dehydrate for the

TABLE II—WATER BALANCE DATA AND MCCLURE-ALDRICH TEST FOR SUBJECT R M

Date	Body weight gm	Total available water intake gm	Total water output gm	Water balance gm	Plasma chlorides mg/100 c cm	CO <sub>2</sub> comb power vol %	Total plasma proteins gm/100 c cm	McClure Aldrich test forearm min
Preliminary period Mar 17	59009	2007	2034	+63				60
Mar 18	59076	2302	2300	+2	592		7.0	71
Dehydration period Mar 19	59104	651	081	-1430				95
Mar 20	57.05	651	1961	-1311				12
Mar 21	5639	651	1307	-656	603	60.5	8.5	10
				(Total negative water balance for 3 days 1397)				
Recovery period Mar 22	55764	3030	798	+2231				77
Mar 23	55020	3401	240	+2161				64
Mar 24	55000	3111	3111	+100				87
Mar 25	59126	0.4	2269	-245				83
Mar 26	58891				601	58.5	7.6	67

# THE MCCLURE-ALDRICH TEST IN WATER BALANCE

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THE intradermal salt solution test was introduced in 1923 by McClure and Aldrich (1, 17) as "of value in determining the so called pre-edematous state of the tissues in nephritis. It has been extensively studied since then in relation to edema (10, 11, 14, 20) fevers, (4, 5, 12) toxemia of pregnancy (15) thyrotoxicosis (9, 18) and jaundice (19). In 1927 Appel and Brill (2) first proposed its use in estimating the state of hydration of patients. Recently Hopps and Christopher (13) employed the test in following the postoperative water balance of 7 surgical patients and stated that it was a sensitive and reliable index of the degree of hydration provided that the electrolyte balance had been taken into consideration. Our experience has not substantiated this opinion.

## CONTROLLED DEHYDRATION STUDY

In the course of previous investigations in this laboratory on the water exchange of surgical patients, dehydration was produced in two normal individuals by limiting their water intake. Both subjects received an adequate maintenance diet of low water content, the mineral content was essentially constant. The full details of this experiment have been published previously (8) with the exception of the McClure Aldrich tests which are reported at this time.

The technique which was used in performing the test was the same as described by the originators: 0.2 cubic centimeter of an 0.8 per cent saline solution was injected intradermally at the volar surface of a forearm and the anterior surface of a leg. Table I shows the water balance and McClure Aldrich tests of subject J. N. Table II the same for subject R. M. Contrary to the expectations of Hopps and Christopher and others (16) who look for a more rapid disappearance of the wheal with

dehydration, more time was needed for these two normal subjects to absorb the salt solution when dehydration was present than for the preliminary hydrated period. Furthermore, no consistent reduction in the disappearance time occurred in the recovery period.

## STUDIES ON NORMAL INDIVIDUALS

White and Irvine Jones have emphasized the variations in the disappearance time of the McClure-Aldrich test in normal individuals. In addition, Wohl and Ettelson reported that there were wide variations in fat individuals in different areas at the same time. Our subject J. N. also showed considerable differences between the disappearance times on the forearm and the leg. To learn more of these differences at first hand a series of the tests were run on 5 patients with local lesions but in good general health, who were taking a full general diet and as much water as they pleased. Table III shows the findings in these cases. It will be noted that wide variations occurred between the disappearance times in different individuals, between the different locations on the same subject, and between successive days in the same location on the same individuals. As much as a 40 minute variation was occasionally found between the tests.

## STUDIES ON SICK SURGICAL PATIENTS

A series of carefully controlled studies of the water and electrolyte balance of sick surgical patients was next carried out in the hope that, in spite of the wide variations found in normals, the McClure Aldrich test might show significant variations associated with changes in either the water balance or the plasma chemistry which would be of clinical value. A few of the most representative cases are herein reported.

Table IV shows the water balance, plasma chemistry studies and McClure-Aldrich tests on patient C. D. a 64 year old man with

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TABLE V—WATER BALANCE, PLASMA CHEMISTRY STUDIES AND McCLOURE-ALDRICH TEST FOR PATIENT C B

24 hours ending	1940	1—4	1—5	1—6	1—7	1—8	1—9
Body weight	gm	67601	64940	63601	65483	65303	66577
Intake	c cm						
Water by mouth			500	500	1150	1800	900
5% glucose I V					2876		1946
Ringer's solution I V					1500		2000
5% NaHCO <sub>3</sub> I V					250		
10% glucose I V					400	200	
Output	c cm						
Bile			1330	820	950	500	1580
Blood			23	23	23	23	23
Urine			440	92	1320	200	1520
Specific gravity of urine			1.013	1.020	1.006	1.015	1.003
Total intake	c cm		500	500	6176	2000†	4846
Total sensible output	c cm		1793	935	2293	723	3123
Plasma chlorides	mg /100 c cm	609	587	566	550	567	573
Carbon dioxide combining power	vol %	26.2	24.7	21.7	43.3	37.8	40.0
Total plasma proteins	gm /100 c cm	5.75	6.70	7.14	5.99	6.19	5.31
NaCl in urine	gm		2.530	0.644	1.637	0.472	1.272
McClure Aldrich test	min						
Right forearm		?	43	29	49	30	23
Left forearm		62	88	36	52	30	32
Right shoulder		63	88	59	60	44	42
Left shoulder		77	88	58	67	65	65
Average		66	77	45.5	57	42.2	40.5

†Value incomplete because patient was on general diet which was not measured

take intravenously to replace her fluid and electrolyte losses and at the end of this 24 hours she was well hydrated, her weight was within a kilogram of the original, but the average of the skin tests was only 40.5 minutes, which was 25 minutes less than the starting values. Summarizing this case there were discrepancies in the relationship between the degree of hydration and the McClure-Aldrich test which seemed to make the latter unreliable.

Table VI shows the data for a 63 year old male with pyonephrosis and uremia. On admission he was comatose and showed signs of marked dehydration and acidosis. The general examination was otherwise essentially negative except for the urine which was found to be loaded with red and white blood cells and a mixed bacillary and coccal infection.

An examination of Table VI shows that the situation is a complicated one, the carbon-dioxide combining power remained below normal throughout the study, the plasma chlorides decreased in the 4 days from 521 to 431 milligrams per cent, considerable sodium chloride was excreted in the urine daily, the urine output was high, yet on January 7 there was a gain of 2.3 kilograms which, since his caloric intake was insufficient, must have been due to water and salt retention. In spite of all these variations the McClure-Aldrich test on January 5, the beginning of the study, was not much different from that on January 8, the end of the study, and one can deduce little from it in relation to the rest of the findings.

The next case, Table VII, is that of a 33 year old female who on admission was mark-

TABLE III.—McCLURE-ALDRICH TEST ON NORMAL PATIENTS

Patient										
	F A min.	S H min.	F A min.	S H min.	F A min.	S H min.	F A min.	S H min.	F A min.	S H min.
Jan 18	43		40	75	30	39	37	3	13	34
Jan 19	15	3	5		45	46	5	3	40	66
Jan 20	39	82	43	95	49		95	95		40
Jan	33	37	30	13	31		36	31	33	33
Jan	40	79	48	77	34	39	33	87	30	45
Jan	49	64	6	32	46		13	3	47	46
Jan 4	30	64	2	21	33	46	11	66	35	60

F A—Forearm

S H—Shoulder

next 3 days by limiting the fluid intake to 500 cubic centimeters of water by mouth daily. After the January 5 period when she had lost 2661 grams in weight the average of the McClure Aldrich tests showed a rise to 77 minutes from 66 minutes. On January 6 the weight decrease was 1339 grams and the McClure Aldrich test dropped to an average of 45.5 minutes which according to Hopps and Christopher would be an indication of de

hydration. On January 7 when replacement therapy was largely given intravenously the McClure Aldrich test approached the normal. On January 8 the patient was allowed to take only what she wished to eat and drink with the result that her intake was not adequate and she voided only 200 cubic centimeters of urine. At the end of this period the skin test showed a drop to an average of 42.3 minutes. The patient was again given an adequate in-

TABLE IV.—WATER BALANCE, PLASMA CHEMISTRY STUDIES AND McCLURE-ALDRICH TEST FOR PATIENT C D

Date 1-29		1-25	1-26	1-26
Body weight	gm	14610	14770	14630
Intake	cm			
5% glucose 1 V		2990	2990	2915
Water 1 V			1494	200
Output	cm			
Vaginal secretion			000	250
Urine			2190	2000
Specific gravity of urine			004	000
Total intake	cm		444	3115
Total sensible output	cm		4790	3050
Plasma chloride	mg / 100 c.c.m			130
Carbon dioxide combining power	vol %	47		
Total plasma proteins	gm / 100 c.c.m	97	40	43
NaCl in urine	gm		76	4.20
McClure-Aldrich test	min			36
Right forearm		37		
Left forearm		37		
Right shoulder		45	70	70
Left shoulder		36		
Average			20.5	39



TABLE VI.—WATER BALANCE, PLASMA CHEMISTRY STUDIES AND McCLURE ALDRICH TEST FOR PATIENT G. B.

hours ending	0-24	2-5	5-6	6-12	12-24	24-48
Body weight	gm	64,397	64,395	67,611	67,653	66,505
Intake						
5% glucose I.V.	cm	1,000	700	20,00	2000	1000
5% NaHCO <sub>3</sub> I.V.			500	50	50	
Range solution I.V.				150		1,100
Normal saline I.V.						500
Food I.V.						500
Output	cm					
Urine			30	1,00	155	
Stool					75	50
Urine			1,600	115	2,700	1,115
Specific gravity of urine	cm		807	804	805	805
Total intake	cm		3,400	7600	6750	6000
Total venous output	cm		1830	2,100	2,820	1,665
Plasma chloride	mg / 100 cm		427	43	43	331
Carbon dioxide combining power	cc %	2	24	23	20	25
Non-protein nitrogen	mg / 100 cm	100		77	8	100
Total plasma proteins	gm / 100 cm		6	10		10
KCl in urine	gm		247	100	570	20,752
McClure-Aldrich test	mls					
Right forearm		66	—	—	10	
Left forearm		—	80	80	—	
Right shoulder		80	90	65	8	
Left shoulder		80	65	80	80	
Abdomen		80	90	5	90	
Average		77	81	7	66	

† Given before test started

edly dehydrated. Although the history was unreliable it was felt that the patient most probably had had ergot poisoning due to drug therapy 9 months previous to admission. A left mid thigh amputation for gangrene of the left leg had been done, and on admission there was gangrene of the right great toe and of the right middle finger. No wrist pulsations could be felt but her circulation showed no evidence of impairment above the elbows. With the hydration of the first 24 hours the patient gained 3.7 kilograms and the plasma chlorides increased approximately 100 milligrams per cent to reach a level close to normal. The urine output was good and sodium chloride was excreted by the kidneys. In spite of this the time for the McClure Aldrich tests was

far below normal before treatment was given and remained so after hydration. Cohen and his co-workers (6, 7, 21) showed that there was more rapid absorption of the intradermal salt wheal in areas with disturbed peripheral circulation and this condition may have been present on the forearms but there was no indication of disturbed circulation in the shoulder region where far below normal readings persisted. There was no apparent significance of the McClure Aldrich test in relation to the water and electrolyte balance of this patient.

## SUMMARY

Although Appel working with Brill in 1927 (2) first advocated the use of the McClure Aldrich test as an index of water metabolism

# THE VENOUS CIRCULATION IN THE LOWER EXTREMITIES DURING PREGNANCY

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LOCAL disturbances in the venous circulation of the lower extremities are quite common both during and immediately following pregnancy. Such disturbances are manifested by the development of varicose veins or the aggravation of varicosities already present, by the appearance of edema in which cardiac, renal, nutritional, or endocrine causes are obviously lacking, and by the occurrence of acute thrombophlebitis, usually as a postpartum complication.

That the state of being pregnant is influential in the production of edema and varicose veins in the lower extremities is generally recognized. The mechanism responsible for these symptoms, however, has never been clearly demonstrated. The symptoms are entirely absent in many patients, are mild in others, and are severe in still others. That some anatomical or physiological factor or "peculiar predisposition" exists in some pregnant women but not in others is suggested by the variability of time of onset, extent, and course of the edema and varicose veins. Since such manifestations are common complications of pregnancy in all races and all classes it does not seem logical to assume the existence of any "peculiar predisposition," such as congenital weakness of the valves of the venous system.

Certain physiological changes occur during pregnancy that might alter the venous circulation in the lower extremities. It is generally accepted that there is an increase in the total blood volume. There is also an increase locally in the volume of blood in the pelvic veins. This is due partly to the augmented vascular supply incident to growth of the uterus and partly to the formation of arterio-

venous communications in the placenta. These physiological changes are found in every pregnancy and consequently do not explain the variability of occurrence of varicose veins and edema. Furthermore, such changes are hardly of sufficient magnitude to account for these symptoms in any case.

Changes in the anatomy of the pelvic organs during pregnancy produce considerable obstruction to the venous return from the lower extremities. Furthermore, the anatomical changes are variable. The position and size of the uterus, the length and mobility of the supporting ligaments, the size of the pelvis, and the tone and development of the abdominal muscles, all may vary to some degree in different pregnant women. Such anatomical variations may account for differences in the degree of obstruction to the outflow of blood from the lower extremities. In some women the obstruction may be sufficient to produce varicose veins and edema.

If obstruction of the femoro-iliac veins is the principal factor in the pathogenesis of edema and varicose veins in pregnant women, it is logical that the most direct approach to the early detection of these disturbances might be by measurements of the blood pressures in the veins of the lower extremities. It seems probable also that such measurements might yield a more complete explanation for the clinical inconsistency of varicose veins and edema in pregnant women. Burwell has demonstrated that the pressures in the femoral veins recorded with the patients in the supine position increase progressively during pregnancy, without any significant change in the venous pressures in the upper extremities, and that delivery is followed by prompt restoration of the pressures to normal. We have confirmed these findings. However, the height of the femoral venous pressure recorded with the patient lying down cannot be correlated

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- Geiss, NIEDMAYR, H., and HILSCH, P. Über den nach-eislatenten Oedem am dem Verhalten Intracutaner Quaddeln einer Normomhoerung. Klin. Wchnschr. 1926, 5, 704.
- HARRISON, J. Intradermal salt solution test in lobar pneumonia in children. J Am M Ass. 1935, 84, 58.
5. HOFFA, H. C., and CHRISTOPHER, F. The McClure-Udrich test in water balance following operation. Surg. Gynec. & Obst. 1930, 69, 637.
4. KENDER, M. M. Edema. I. Correlation of elastometer findings, disappearance time for intradermally injected salt solution, urinalysis and nitrogen retention of the blood in edema. Arch. Int. Med. 1926, 38, 57.
5. LASKI, H. F. Intradermal salt solution test in normal and toxicemic pregnancies. Surg. Gynec. & Obst., 1926, 43, 40.
6. LEROUX, M., and PETRASOVITCH, A. L'épreuve intradermique à l'eau salée physiologique. Nourisson, 1933, 4.
7. McCLELLAN, W. B. and ALLEN, C. A. Time required for disappearance of intradermally injected salt solution. J Am. M. Ass. 1935, 8, 203.
8. MORA, J. M. The intracutaneous salt solution test in thyrotoxicosis. Am. J. M. Sc., 1926, 77, 0.
9. MORA, J. M. and JURETA, F. J. The effect of jaundice on intradermally injected salt solution. J. Lab. & Clin. Med., 1935, 20, 19.
10. OLSEN, H. C. Intradermal salt solution test in cardiac disease in children. Arch. Int. Med. 1926, 37, 28.
11. STERN, W. G., and COHEN, M. B. The intracutaneous salt solution test. Its value in disturbances of the circulation of the extremities. J Am. M. Ass., 1926, 87, 355.
2. WHITE, H. L., and IRVING JONES, E. Factors affecting the disappearance time of intradermal injections. Am. Heart J. 1937, 15, 7.
3. WOOD, M. G. and ETTLESON, L. N. Water retention in obesity as determined by the McClure-Udrich test. J. Lab. & Clin. Med. 1936, 21, 300.

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The column of mercury in the manometer will quickly come to a level which indicates the local blood pressure in the vein. The height of this level is recorded as the initial

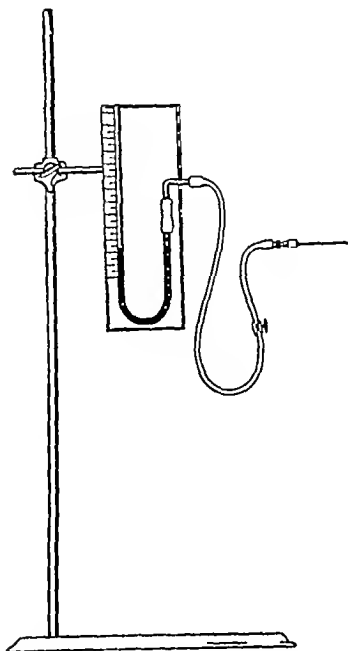


Fig. 1. Mercury U tube for measurement of popliteal venous pressure. Connection to popliteal vein through closed system.

venous pressure. The patient then begins the exercise which consists in rising on her toes repeatedly (20 to 30 times) for 1 minute. It is important that she use the wall supports for her hands only for the purpose of steadying herself and not as a means of assisting the exertion, that she breathe regularly during the exercise, and that she relax the muscles of her legs each time her heels are lowered to the surface of the table. During the test it is necessary for the operator to support the rubber tubing of the apparatus with his hand in order to keep the needle horizontal and prevent it from slipping. The changes in venous pressure during exercise are recorded, and the pressure is observed for a short time after exercise has ceased. The needle is then withdrawn and firm pressure is applied for about a minute at the site of venipuncture. The patient is required to walk around the room for a few minutes at the conclusion of the test in order to prevent venous thrombosis.

In normal individuals and in patients with edema of the lower extremities due to nephrosis, nutritional deficiency, or lymphatic ob-

with the occurrence of varicose veins and edema. Thus patients with marked edema and varicose veins may have lower femoral pressures recorded in this way than some patients who have neither of these symptoms, so that confirmation of venous obstruction as the cause of the symptoms is not obtained.

As far as we have been able to discover from reviewing the literature no attempt has previously been made to measure the pressures in the deep veins of the lower extremities of pregnant women with the patients standing. It must be recognized that such a procedure might elicit evidence of venous obstruction that would be lacking in venous pressure measurements obtained in the usual way. This presumption is based upon the fact that the upright posture apparently aggravates the manifestations of obstruction of the veins in susceptible patients. Furthermore, in patients with edema rest in bed usually relieves the edema, and if varicose veins are present these promptly collapse. For measurement of venous pressures in the lower extremities with patients standing deep veins must be used for accurate results. The pressures in the superficial veins are much too readily influenced by local factors, such as muscular exercise and tone, the state of the veins and the venous valves etc. For reasons that will be obvious later the popliteal vein is most suitable for the purpose in view.

Unfortunately a single measurement of the pressure in the popliteal vein with the patient standing is impossible of interpretation by ordinary means. Only the local pressure (pressure at the level at which the vein is punctured) can be estimated. The reference point for the zero level of the manometer for measurement of the pressure in terms which take into account the hydrostatic pressure is unknown. Even in the absence of localized venous obstruction the local popliteal pressure shows a great and as yet unaccountable variation in different patients. Repeated measurements of the local pressure in the popliteal vein in a pregnant woman might be useful for demonstrating progression of venous obstruction but even this is doubtful. It has been our experience in previous studies (3, 4) that there is no constant relationship

between venous obstruction and the height of the venous pressure measured in the usual way. This is due to the fact that obstruction of the peripheral veins leads to the development of collateral channels which often are adequate to carry away the blood under resting conditions, so that the venous pressure may remain relatively normal. In such cases, however exercise imposes conditions in which the venous collateral circulation may be quite inadequate. For example exercise of an extremity in which the veins are partially obstructed may augment the inflow of arterial blood many times what it is during rest. Then the venous pressure in the affected extremity will rise to a varying degree, depending on the amount of venous obstruction and the extent of the collateral circulation, although it may have been within the normal range before exercise began. These facts led us to devise means for measuring the venous blood pressure during standard exercise tests in patients suspected of having obstruction of the veins of the upper or lower extremity.

The exercise test of venous pressure in the lower extremity entails the use of the popliteal vein. The apparatus (Fig. 1) for measurement of popliteal venous pressure consists of a mercury U tube manometer one arm of which is straight the other arm bent at an angle to facilitate attachment of a piece of rubber tubing. A millimeter scale is affixed beside the straight arm for purposes of recording pressures. Measurements obtained on this scale of course must be doubled in order to represent true records of pressures in terms of millimeters of mercury. The other arm is filled completely from the surface of the column of mercury to its tip with 2.5 per cent sodium citrate solution. The height of the column of mercury beside the millimeter scale is noted. Next a sterile length of rubber catheter tubing having a needle adaptor in one end is filled completely by means of a sterile 5 cubic centimeter syringe with sterile 2.5 per cent sodium citrate solution. This tubing is clamped with a small hemostat and its free end is then slipped on the designated arm of the manometer care being taken to exclude air bubbles from the system. The manometer is adjusted on its supporting stand

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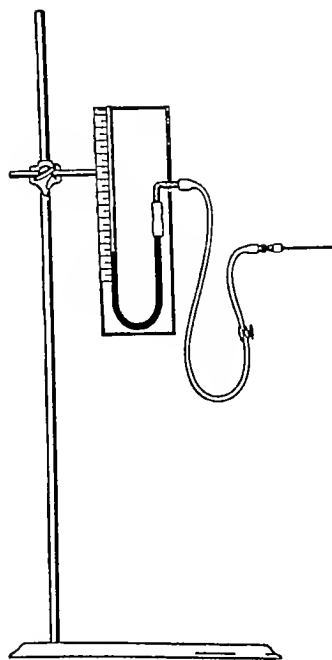


Fig 1. Mercury U tube for measurement of popliteal venous pressure. Connection to popliteal vein through closed system.

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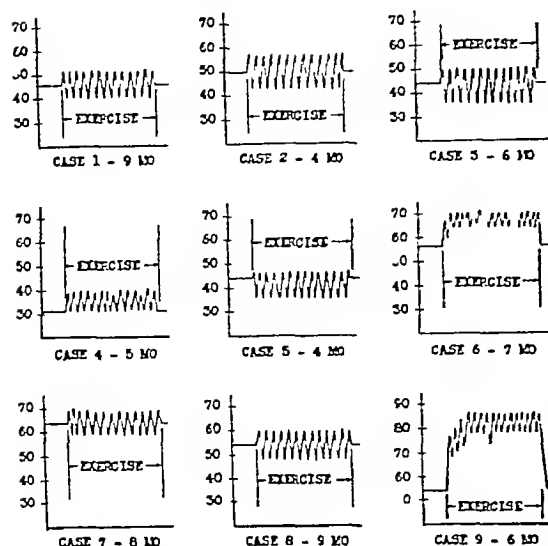


Fig 4 Popliteal venous pressures (mm of mercury) in pregnant women having no edema or varicose veins. Note the uniformity of patterns except in Cases 6 and 9.

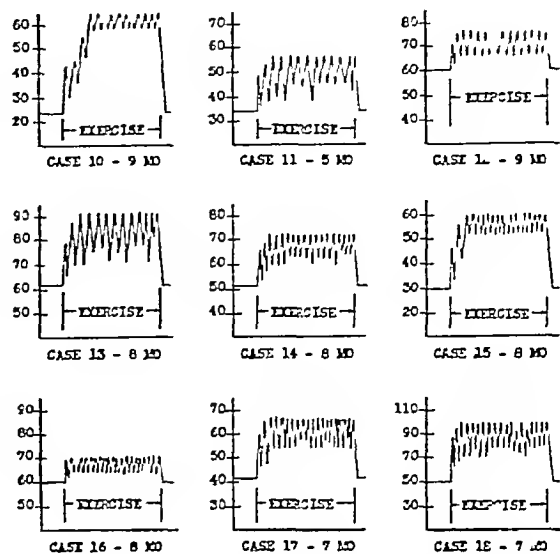


Fig 5 Popliteal venous pressures (mm of mercury) in pregnant women having edema and/or varicose veins. Note uniformity of patterns.

while the 16 others, or 44 per cent, had edema, or varicose veins, or both. Fourteen of the women, 39 per cent, were primiparas, and 22, 61 per cent, were multiparas. Only 4 of the 14 primiparas, 29 per cent, had edema or varicose veins or both, while 12 of the 22 multiparas, 55 per cent, had these manifestations. Although the group is small, this higher incidence of such manifestations in multiparas is in keeping with the general experience of obstetric practice.

Because of the social level of the patients attending the clinic at which our studies were made, comparatively few patients were observed early in pregnancy (Fig 3). Thus only 1 of the 36 patients was in the first trimester, 10 were in the second trimester, and the 25 remaining were in the final trimester. The single case observed during the first trimester had neither edema nor varicose veins, but 15 of the 25 in the third trimester, 60 per cent, had edema and/or varicose veins. The higher incidence of these manifestations in the latter months of pregnancy again is in accord with usual obstetric experience.

In each case a recording of the initial pressure in the popliteal vein was obtained with the patient standing quiet, after which the

"exercise test" as herein described was performed. There was no immediate correlation between the initial pressures and the presence of edema or varicose veins (Fig 3). In fact, the 3 lowest initial pressures were recorded in patients with edema and varicose veins. Of the 20 patients having neither edema nor varicose veins, 18, or 90 per cent, showed normal patterns of the popliteal venous pressure during exercise. That is, the pressure fluctuated above and below the initial pressure or oscillated between the initial pressure and a reading not more than 8 millimeters of mercury above the initial pressure. Figure 4 demonstrates examples of the normal patterns obtained in these cases, except Cases 6 and 9. In these 2 cases, 10 per cent, the response of the popliteal venous pressure to exercise followed an obstructive pattern. In Case 6, after an initial reading of 56 millimeters, the venous pressure fluctuated during exercise from 64 to 70 millimeters. In Case 7, the initial reading was 54 millimeters, during exercise the pressure ranged from 68 to 86 millimeters.

In the 16 patients having edema or varicose veins or both, obstructive patterns of response of the popliteal venous pressure during exer-

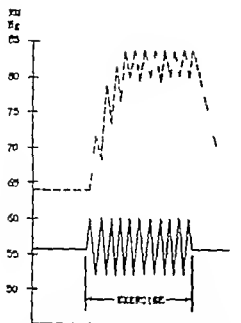


Fig. 1. Popliteal venous pressure in case of right femoro-iliac thrombosis. Demonstrates contrast of obstructed and nonobstructed legs. — left leg ——— right leg

struction, the popliteal venous pressure is little affected by the exercise described. The column of mercury in the manometer fluctuates usually above and below its initial level through a distance of 8 to 12 millimeters but shows no tendency to rise progressively. On the other hand, in patients having significant obstruction of the femoral or iliac veins due to thrombosis compression by tumor or other cause the popliteal venous pressure, in addition to oscillating with each movement of the patient as she performs the prescribed exercise tends to rise progressively. The amount of rise theoretically should depend mainly upon the degree to which there is delay in the outflow of blood through the obstructed veins. However it has been our experience that the pattern which can be traced from the response of the venous pressure to the exercise imposed is of more practical importance than the amount of rise. In other words a pattern which shows only oscillation of the pressure above or below the initial venous pressure indicates that the venous system is adequate under conditions

mm Hg	MONTH OF PREGNANCY								
	1	2	3	4	5	6	7	8	9
70									
60									
50									
40									
30									
20									

Fig. 2. Initial popliteal venous pressures in 36 pregnant women. Not a measure of correlation between height of column pressure and edema or varicose veins. O Patients with edema or varicose veins, ● patients with edema and/or varicose veins

of the test while a pattern which shows a progressive rise of the pressure to any degree in addition to the same type of oscillation, indicates that the venous system is inadequate. Figure 2 presents the contrast of the two types of pattern. In this case of femoro-iliac thrombosis of the right side the popliteal venous pressures clearly demonstrate the presence of venous obstruction in the right leg and the absence of obstruction in the left leg.

It was our interest in the preparation of this present report to apply the procedure of measurement of popliteal venous pressure with the patient standing and during exercise to pregnant women as a part of the search for an explanation of the cause of varicose veins and edema.

#### CLINICAL RESULTS

Thirty-six pregnant women were studied in the order of their admission to the prenatal clinic in the outpatient department at the Gallinger Municipal Hospital. No attempt at case selection was made but no patient in the group had any detectable toxemia or other complicating illness. All of the patients were of the negro race. Twenty of the 36 or 56 per cent had neither edema nor varicose veins,

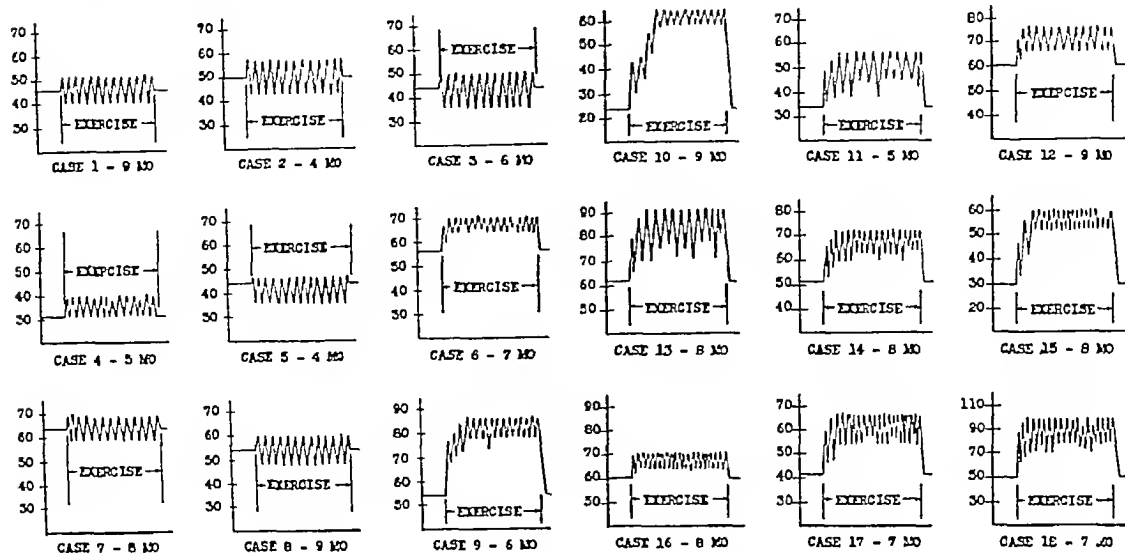


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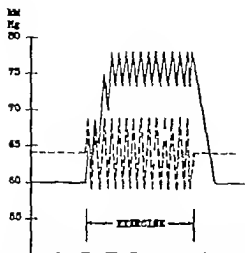


Fig. 6. Popliteal venous pressures in pregnant women having edema of the left leg only. Note normal pattern in nonedematous leg and obstructive pattern in edematous leg—left leg—right leg.

cise were obtained in all cases. Figure 5 gives some examples of these patterns. In 2 of these cases (Cases 12 and 16) the fluctuations of pressure during exercise were of relatively low order possibly indicating that the venous obstruction was of milder degree. In the 14 remaining patients, patterns typical of severe venous obstruction were obtained during exercise. For example in Case 10 the fluctuations of pressure reached peaks of 40 millimeters of mercury higher than the initial pressure of 24 millimeters. In Case 5 the oscillations were 22 to 30 millimeters and in Case 18 20 to 40 millimeters higher than the initial pressure. In one other case not shown in the figure the peaks of the oscillations were 56 millimeters higher than the initial popliteal venous pressure.

#### EVALUATION

The assumption that postural dependent edema and varicose veins in pregnant women are due mainly to compression of the iliac veins by the enlarging uterus or as the result of other anatomical changes, has always had some clinical substantiation. However it has been difficult to reconcile with this assumption the fact that all pregnant women do not develop these manifestations. Venous pres-

ures measured in the usual manner in the femoral veins with the patients supine do not differ significantly in the group of women with supposed evidence of venous obstruction and the group without such clinical evidence. Although the complete reconciliation of these facts has not been achieved, the original assumption has been sustained by the patterns obtained by the measurement of the pressures in the popliteal veins during exercise. In addition it has been learned that in pregnant women who show varicose veins or edema of the type under discussion there actually is a more severe degree of venous obstruction than in women who are free of these symptoms. Failure of femoral venous pressure determinations of the usual type to demonstrate this difference must be ascribed to the incompleteness of the procedure. It does not take into account the facts that a venous system may be adequate during rest and grossly inadequate under conditions of ordinary activity and that an upright posture may play a large part in aggravating obstruction of the venous flow from the lower extremities.

Further clinical proof of the obstructive origin of edema and varicose veins during pregnancy is found in the occasional case in which the symptoms are strictly unilateral. For example, in one patient of the group studied there was moderate edema of the left lower extremity without edema of the right at the eighth month of pregnancy. This kind of phenomenon would be difficult to explain except as the result of obstruction of the left iliac vein and indeed the patterns obtained on measurement of the popliteal venous pressures during exercise (Fig. 6) support the clinical evidence. The pattern from the left popliteal vein is one of venous obstruction, while that from the right popliteal vein is normal. This case and the type of case in which edema or varicose veins are most prominent during the early months of pregnancy and tend to regress as pregnancy continues strongly suggest that the position of the uterus may be important in the pathogenesis of localized obstruction of the deep veins. However speculation as to the anatomical or other factors responsible for heightening the degree of occlusion of the veins in pregnant women who develop the

symptoms discussed here cannot be very fruitful in the absence of additional careful studies of the anatomy and physiology of the venous system

In our opinion, measurements of the popliteal venous pressures during exercise in pregnant women who show edema of the lower extremities yields information which is essential to the care of the patient. If the venous pressure pattern is not of the type found in cases of venous obstruction, some other cause for the edema should be sought. On the other hand, if an obstructive pattern is obtained, care of the patient should be directed to the prevention of varicose veins. One of us (2) has shown that protection of the superficial veins by means of elastic stockings will prevent or greatly minimize the development of varicose veins in patients having localized obstruction of the femoro-iliac veins. The stockings are even more useful in pregnant women than in some other cases because the duration of venous obstruction is relatively so much shorter. If the superficial veins are protected in this way, their valves remain intact and varicose veins are consequently less likely to appear.

#### SUMMARY AND CONCLUSION

1 The assumption that postural dependent edema and varicose veins of the lower extremities in pregnant women are due to

localized obstruction of the deep veins is supported by the types of pressure curve obtained when popliteal venous pressures are recorded during exercise

2 The factors responsible for increasing the degree of localized venous obstruction in some pregnant women to the point of causing edema or varicose veins or both are not perfectly understood. The size and position of the uterus are factors of recognized importance

3 In pregnant women manifesting significant obstruction of the femoro-iliac veins, provision of adequate support for the superficial veins by means of elastic stockings minimizes or prevents the development of varicose veins

We wish to thank the members of the Department of Obstetrics of the Gallinger Municipal Hospital for their co operation in these studies

#### REFERENCES

- 1 BURWELL, C. S. A comparison of the pressures in arm veins and femoral veins with special reference to changes during pregnancy. *Ann Int Med.*, 1938, 11: 1305
- 2 VEAL, J. R. The mode of development of collateral venous circulation in the extremities. *Am Heart J.*, 1940, 10: 275
- 3 VEAL, J. R., and HUSSEY, H. H. The use of "exercise tests" in venous pressure measurements for the detection of venous obstruction in the upper and lower extremities. *Am Heart J.*, 1940, 20: 308
- 4 Idem. Methods for measurements of pressures in the antecubital and popliteal veins during exercise. *M. Ann District of Columbia*, 1940, 9: 71

# PERSISTENCE OF FUNCTION OF SKIN GRAFTS THROUGH LONG PERIODS OF GROWTH

JAMES BARRETT BROWN, M.D., F.A.C.S., and FRANK McDOWELL, M.D.  
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**F**UNCTION has been found to persist in large skin grafts that have been in place during long periods of growth and the fundamentals that have proved of value in carrying out large surface repairs are reviewed here.

Both thick split and full thickness grafts do seem to grow or at least stretch out with growth of the body area and to permit normal movement if they have been successful from the start. This has been true in many patients and over areas of the body from the face to the feet (Figs. 1 to 10).

There is a condition that may be called *generalized skin shortening* of an area in which there is no evident distortion but a definite lack of flexibility and ease of function. This may result from failure of releasing the scar sufficiently or from growth of the area without enough enlargement of original grafts. The

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Presented before the Western Surgical Association, Topeka, Kansas, December, 1940.

condition may be likened to clothes that are too tight or it may be said that the skin envelope is too small. This means that *scar and its contracture persist until released*. If it is completely released early in life, the repair should last. If with increased growth, the shortening does appear, then more skin can be let in by simply opening the tightest area, allowing the edges to retract and filling the resultant defect with suitable grafts. Where the scar tissue is very thick, however, the edges will not retract when opened and then large areas have to be excised down to good soft tissue and still larger grafts applied (Figs. 6 and 10).

By *satisfactory late function of the grafts* is meant (1) enough skin for free movement (2) moderate looseness (3) ability to withstand the usual trauma of getting around (4) the development of normal sensation. Full normal sensation usually develops in free skin grafts and is influenced by the amount of deep scar that is left and, of course, is dependent on there being sensory nerves in the area.



Fig. 1. Extreme deformity of neck and jaw corrected by thick split graft and full thickness graft operations. Recorded after an 8 year period of growth with complete

restoration of contour. Surface smoothness can be improved with further grafts; but patient takes both also repaired.

*Metaplasia* of grafts (and flaps also) does not take place and, therefore, a really normal sole of the foot, for instance, cannot be restored. This area is specialized to the point of being an organ, the skin and subcutaneous tissues are different from birth and the peculiar bearing qualities are not developmental. A graft or a flap on a sole may make calluses (or even annoying warts) but it will not *metaplasia* into true skin or subcutaneous tissue of the area. They always have to be protected and the wart formation guarded against (Figs 4 and 9). If hair is transplanted, it will continue to grow, except that it may be worn off.

Skin grafts transplanted to normal mucous membrane surfaces, such as the mouth, larynx, and eye socket, show no evidence of a change to a mucous membrane. The skin simply persists as such and even raises hair in these areas if there are any functioning follicles in the graft.

*The results of grafting vary in different regions and with the type of lesion.* A graft put on a soft base with a good blood supply can be expected to be more certain than if put over the shin or ankle where there is little deep pad

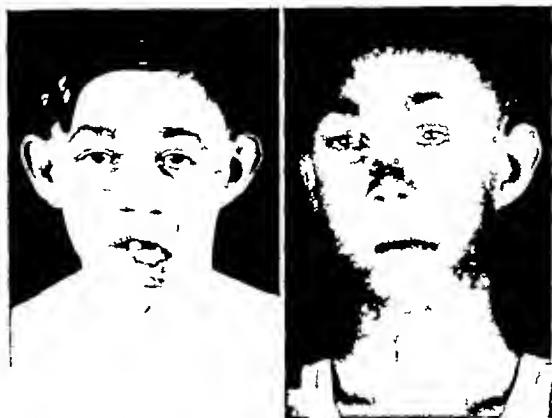


Fig. 2. Difficult contracture of mouth and neck, repaired with three thick split grafts from clavicle to level of nose. Contour has remained satisfactory after 13 year growth period.

to help absorb shocks and trauma. Likewise, an old x-ray burn or leg ulcer with deep and surrounding fibrosis and lack of resiliency of the tissues cannot afford as good a bed or area for a graft as a simple burn. Old chronic leg ulcers with deep scarring and edema tend to recur, so that improvement of local circulation is necessary if the repair is to prove efficient, the graft itself, of course, may assist in this

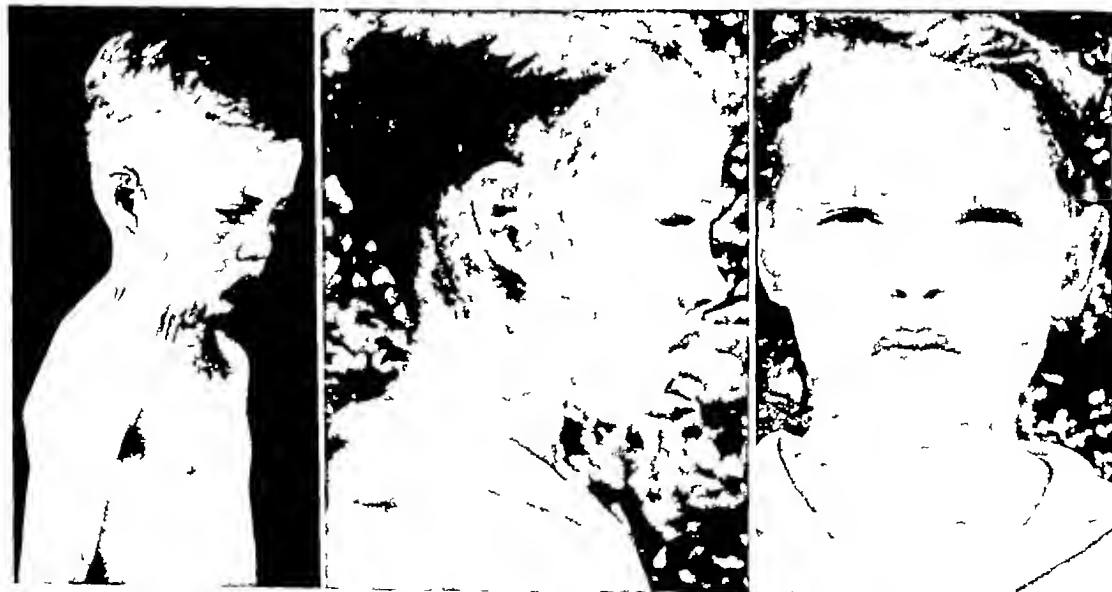


Fig. 3. Marked distortion and jaw twisted down into open bite, corrected in 2 split graft and 2 full thickness

operations. Normal profile and occlusion of teeth resulting and recorded a second time after 10 year period of growth.

# PERSISTENCE OF FUNCTION OF SKIN GRAFTS THROUGH LONG PERIODS OF GROWTH

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**F**UNCTION has been found to persist in large skin grafts that have been in place during long periods of growth and the fundamentals that have proved of value in carrying out large surface repairs are reviewed here.

Both thick split and full thickness grafts do seem to grow or at least stretch out, with growth of the body area and to permit normal movement if they have been successful from the start. This has been true in many patients and over areas of the body from the face to the feet (Figs. 1 to 10).

There is a condition that may be called *generalized skin shortening* of an area in which there is no evident distortion but a definite lack of flexibility and ease of function. This may result from failure of releasing the scar sufficiently or from growth of the area without enough enlargement of original grafts. The

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condition may be likened to clothes that are too tight or it may be said that the skin envelope is too small. This means that *scar and its contracture persist until released*. If it is completely released early in life the repair should last. If with increased growth the shortening does appear then more skin can be let in by simply opening the tightest area, allowing the edges to retract and filling the resultant defect with suitable grafts. Where the scar tissue is very thick however the edges will not retract when opened and then large areas have to be excised down to good soft tissue and still larger grafts applied (Figs. 6 and 10).

By *satisfactory late function of the grafts* is meant (1) enough skin for free movement (2) moderate looseness (3) ability to withstand the usual trauma of getting around (4) the development of normal sensation. Full normal sensation usually develops in free skin grafts and is influenced by the amount of deep scar that is left and, of course, is dependent on there being sensory nerves in the area.



Fig. 1. Extreme deformity of neck and jaw corrected in thick split graft and full thickness graft operations. Recorded after 8 year period of growth. With complete

restoration of contour. Surface smoothness can be improved with further grafts when patient takes Pock villas also repaired.

scribed What would be a good functional result on a leg or axilla would be a very poor one on the face, because of roughness and pigmentation However, the same general rule applies for a late, desirable cosmetic result as for function if the graft has been satisfactory soon after operation, it will probably persist as such The unevenness and wrinkling can be minimized by careful dissection of the base and by using full thickness rather than split grafts However, chances of too much pigmentation persist without relief at the present time, and the patients may have to rely on the application of cosmetics (Figs 1, 2, 3)

By studying these patients several years after operation, the fundamentals of treat-



Fig 7a

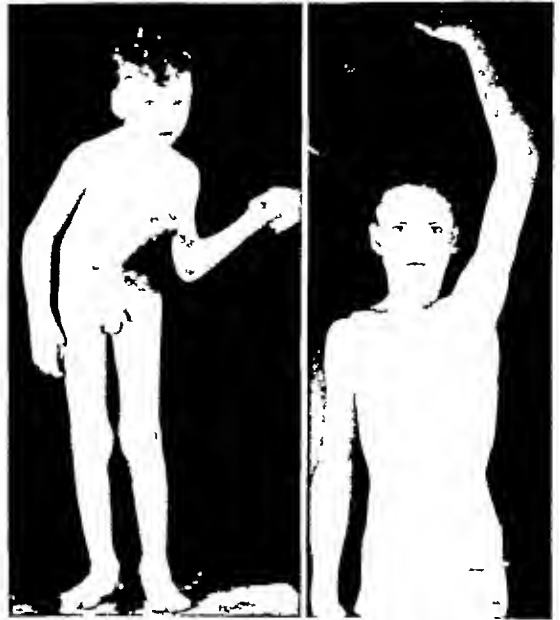


Fig 6 Very deep, widespread burn Patient tied over critical period with large, split homografts from mother Axilla then released in 2 split graft operations Generalized skin shortening across abdomen and flank released 2 years later with split grafts Normal function recorded a second time, 9 years after operation Grafted area extends from iliac crest all the way up through axilla and down over arm

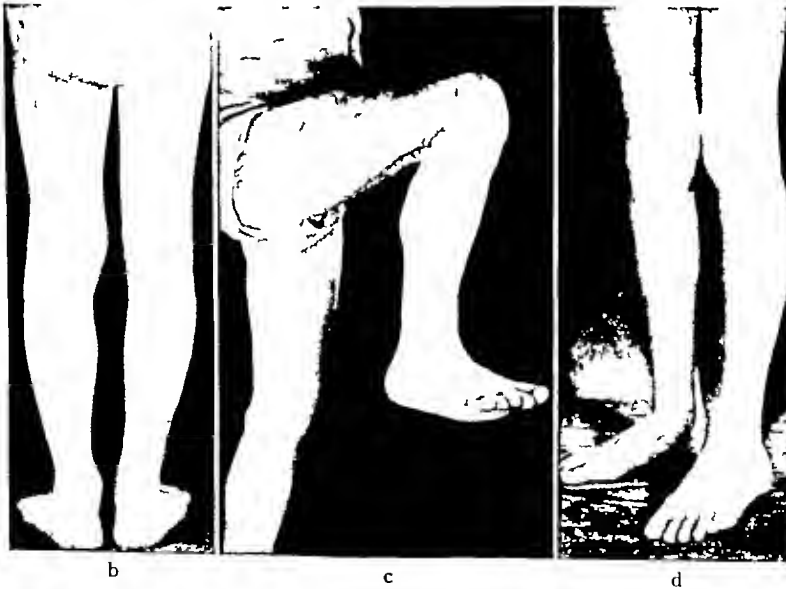


Fig 7 a, b, c, Complete circular loss repaired in 3 split graft operations Shown after 2 years d, Same type of burn 8 years after 1 single operation



Fig. 4. Replacement in operation, his full thickness graft of entire palmar surface of hand and fingers. The graft has definitely enlarged and is satisfactory to the boy in every way after 3 years of growth, following first recording.

A frequent cause of loss of grafts applied for long-standing fibrosed ulcers is failure to remove the scar down to soft tissue; one should avoid denuding bone or tendons in the process, however.

Although grafts and flaps are not being compared, a successful graft may be more apt to continue satisfactorily throughout a growing period than a pedicle flap because flaps have a tendency to hump up and become heavy from fat rather than to spread out.

Cosmetic results with free skin grafts may not be as good as the functional results de-



Fig. 5. One of the most difficult types with heavy distorting scar encasing entire arm and joint. Required split



grafts but complete function of the skin grafts persists after 4 year period of growth.

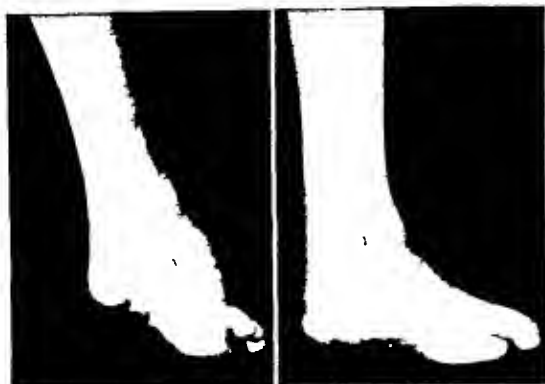


Fig. 9 Restoration in 1 split graft preceded by bone correction by Dr. Crego. Function satisfactory with graft on sole of foot after 9 years of growth. Free grafts can work on the foot only if sufficient deep pad has been left; otherwise, a thick pedicle flap is used.

Any method that leaves behind enough skin for healing, splits through the skin, and for this reason the term "*thick split graft*" has been used. Many other names have been suggested but the term "*thick split*" seems most descriptive. The usual thickness is from one-half to three-fourths of the skin and the thickness can be graduated in cutting with some practice. The thickness of the graft varies in relation to the full thickness of the skin which, itself, varies greatly according to age, nutrition, race, and its position in the body. The actual measurement of the thickness of the graft has to be in relation to these variables. The main essentials are a long, sharp knife and some means of creating a diaphragm of the skin on which to cut.

*Saving a good donor site on badly burned patients* is important for obtaining smooth full thickness grafts when the final operations are to be done about the face and neck. Usually an entire thigh or the lower abdomen can be left for this work, but it is frequently found that pinch grafts have been removed right out of the center of these areas.



Fig. 10 Generalized skin shortening of 26 years' duration that prevented sitting down normally. Relieved with thick split skin grafts and shown after 15 years' duration of function.

With these criteria fulfilled, *huge areas may be grafted*. Up to 600 square inches have been done in one patient and 100 to 200 square inches at a time are possible. To do this, huge grafts are necessary and they have been taken as large as 36 inches by 4 inches. To try to repair large areas with small chips of grafts is uncertain and nerve-racking. Even at best, long operative times are necessary and the condition of the patient must be watched closely.

However, when large areas are grafted at one sitting, the *total* amount of work which must be carried out is greatly lessened (Figs 7 and 8).

It seems definite that large surface repairs can be done successfully with free grafts without resorting to the cumbersome use of flaps in most instances. Growth (or stretching) of the grafts occurs so that, even after the patient has passed through long periods of growth, the restorations are found to be satisfactory.





Fig 8 Complete flexion from split graft operations. Foot drop even though nerve as exposed to dissection.

Patient came in for amputation. Recorded second time after 9 year growth period.

ment for early lesions have been made more clear and may be briefly outlined.

*Repairs of large surface defects if possible should be made early* before debilitation, scarring and contracture have taken place. Most burns can be made clean enough to graft in 3 or 4 weeks, but, if good care is not given the areas, infection pain and debilitation develop and late deaths may occur (Fig 7)

*Homografts* may be used for temporary relief during waiting periods, but these grafts never persist in spite of attention to blood grouping down into the 'm and n subgroups. What does happen is usually a 'take' of the grafts with a period of respite from the painful dressings for several days or weeks. With this there is a general improvement, a clearing up of infection and, because of these things, a stimulation to spontaneous epithelialization. Therefore actual healing may occur even though the homografts are completely absorbed and this process may be so marked that some observers may think the homografts themselves have persisted (Fig 6)

*Pinch grafts or small deep grafts* are used occasionally in areas that are covered by

clothes and have the advantage of not requiring a major operation. However they are unsightly in any area and may be replaced later with larger grafts if desirable

When large areas are to be dealt with consistently it is advisable to develop a *simple direct method of cleaning wounds obtaining large sheets of grafts* of suitable thickness and applying them accurately to insure growth. *The donor site* of these grafts is most important and when large areas are denuded, it is necessary to split through the skin to leave some deep gland elements to dedifferentiate into squamous epithelium so that a new surface may form. With careful dressing of the donor site surface healing will be satisfactory in 12 days. As many as four crops have been taken from the same area and one crop taken 19 days after the previous one. If the reverse is true, that is if the skin is cut through or the donor site becomes infected healing will be delayed for weeks and no subsequent crops can be taken. This is somewhat comparable to the loss of epithelial healing that occurs under an infected tannic acid or silver nitrate crust (Fig 8)

## OBSERVATIONS

There were no deaths in either series. One dog in the second series at the end of the second month developed a sudden increase in weight and what was thought to be ascites. The icteric index suddenly rose, although the animal's clinical condition remained excellent. The fluid wave in the abdomen disappeared just as suddenly and the jaundice receded. At the end of the period of observation the dog was sacrificed, the stomach was hugely dilated and contained several large pieces of bone which apparently had obstructed the pylorus and angulated the common duct.

*Red cells and hemoglobin.* All of the animals developed a drop in the red cell count and hemoglobin concentration. The dogs which had had the gall bladder out in addition to the obstruction showed a marked initial decrease, but after the first week the average variations were insignificant. The series of dogs with just the obstruction showed a slower but similar decline with the leveling of the curve occurring only after 3 weeks. The dogs in which the gall bladder had been removed did not show as great a total drop as those dogs with the obstruction alone.

Each animal over a period of 3 months lost approximately 400 cubic centimeters of blood. This loss in repeated amounts of 30 cubic centimeters does not seem great enough to explain the developing anemia. Snell, Greene, and Rowntree (40), after ligating the common duct and removing the gall bladder, noted a steady fall in the number of red cells with a slight reduction in hemoglobin. They attributed this result to repeated bleeding. Mann and Bollman refer to the anemia that is associated with liver injury. This may have been a factor in the present series in addition to the chronic blood loss.

*Blood clotting.* The coagulation time according to the method of Lee and White (25) was done each time blood was taken. The average coagulation time curve in the series with the gall bladder present showed a slight decrease, but the difference was not great. In general, the coagulation time showed no significant variation. In support of this observation none of the dogs showed any tendency to bleed. Lee and Vincent (24) have stressed the dura-

tion of jaundice as a factor in causing an increase in coagulation time. Since the icterus in these animals lasted only 2 to 3 weeks, a change was not to be expected.

*Icteric index.* In the first series with the gall bladder in place the maximum rise in the jaundice did not occur until the seventh day. When the gall bladder was removed, in addition to the obstruction to the common duct the jaundice was highest in all but 1 of the animals from the third to the seventh day after operation. Thereafter, in both series the icteric index gradually diminished and returned to normal during the period of observation. This acute rise when the gall bladder was absent has been demonstrated previously, it was to be expected, since the gall bladder was not present to store the secreted bile. The speed by which obstruction to the common duct becomes apparent has been demonstrated by Snell and his co-workers (41). They found a direct van den Bergh reaction  $1\frac{1}{2}$  hours after ligation of the common duct and removal of the gall bladder while the serum bilirubin increased to 2.2 milligrams per 100 cubic centimeters in 4 hours.

*Urea nitrogen.* The blood urea nitrogen in both series showed an initial decrease, then a rise between the fourteenth and twenty-first days, and decreased from then to the end of the period of observation. These variations were more marked in the series with the obstruction present and the gall bladder removed. It is difficult to explain why the presence or absence of the gall bladder should make this difference. Since the values for the blood urea nitrogen varied conversely with the icteric index, some degree of temporary hepatic insufficiency is suggested as the cause. If this explanation is valid, the larger variations in the blood urea nitrogen in those dogs which had had the gall bladder removed in addition to the obstruction postulate a greater degree of early hepatic damage in that series. Previous observers have all demonstrated a decrease in the blood urea in the presence of jaundice or after hepatectomy (Yanagi and Bollman, Mann, and Magath).

At the end of the experiments the curves in both series approximated each other. It must be pointed out that all the values are within

## THE EFFECT OF PARTIAL OBSTRUCTION OF THE COMMON BILE DUCT

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PARTIAL or recurring obstruction to the common bile duct in man causes many distressing symptoms. In the absence of stone stricture or cancer these symptoms have been attributed variously to dysfunction of the gall bladder tonic or structural disturbances of the sphincter of Oddi, and inflammation of the pancreas. The differential diagnosis of these conditions, when jaundice is not present is difficult. Any diagnostic help therefore would be a distinct assistance. An attempt was made experimentally to produce a similar condition in the dog by causing a partial obstruction to the common bile duct and to observe the effects.

The first clinical report of "gall-bladder colic" without stone or infection was made by Krukenberg in 1903. Aschoff and Baczmeister (3) in 1909 described what they called the stasis gall bladder distinguishing the hypertrophic and atrophic types, depending on the condition of the muscle layer of the gall bladder. In 1920 Schmieden (38) correlated the pathological with the clinical findings and stressed mechanical hindrances to the flow of bile as the cause of the symptoms. Berg in 1922 found a hypertrophy of the sphincter of Oddi and suggested a functional disorder of this muscle as the cause for biliary stasis. This observation has been confirmed since then by Westphal (48). Nuboe Newman, Giordano and Mann (15). This theory already had been suggested on physiological grounds by Oddi and by Meltzer. Westphal (49) then classified these states as atonic and hyperkinetic with a further differentiation of the hyperkinetic type into hypermotile and hyper-tonic states. More recently several observers have demonstrated a physiological obstruction to the lower end of the common bile duct in man (McGowan, Butsch, and Walters (28).

Ivy (19) Best and Hicken) Similar obstruction caused by pancreatitis has been shown to occur by Thieszen and Walters (43)

### METHOD

In the first series of 5 dogs, under barbital anesthesia and with an intratracheal tube in place, the common bile duct was exposed. It was dissected completely free from surrounding tissue just proximal to its entrance into the duodenal wall. This portion was carefully selected so as to be distal to the juncture of the bile duct from the right lobe of the liver and the common duct. At this point a silver clip was placed around the duct so as to include the duct and a stylet measuring 18 millimeters in diameter. The ends of the clip were pressed firmly together and the stylet was removed, thus allowing the clip to remain in place. The abdominal incision was closed in the usual manner.

In the second series of 5 dogs the same procedure was carried out but in addition a cholecystectomy was performed.

After operation the dogs were rarely sick, and food was taken on the first day. The diet was a standard one of cereal and meat scraps.

Samples of blood were taken in the fasting state before the operation, on the first, third, and seventh days after operation and weekly thereafter for a total of 13 determinations on each dog over a period of 6 weeks. The coagulation time according to the method of Lee and White (23) was done at the time the blood was drawn. The number of red cells and the concentration of hemoglobin was determined. The remaining blood was then analyzed for cholesterol, cholesterol esters, total calcium, urea nitrogen, fibrinogen and serum bilirubin stated as icteric index. The weight of the dog was noted at the time of each blood sampling. All stools were tested for the presence of bile by the Schmidt test to rule out the possibility of complete obstruction occurring.

From the Laboratory of Surgical Research, Department of Surgery and the Institute of Pathology Western Reserve University.

## OBSERVATIONS

There were no deaths in either series. One dog in the second series at the end of the second month developed a sudden increase in weight and what was thought to be ascites. The icteric index suddenly rose, although the animal's clinical condition remained excellent. The fluid wave in the abdomen disappeared just as suddenly and the jaundice receded. At the end of the period of observation the dog was sacrificed, the stomach was hugely dilated and contained several large pieces of bone which apparently had obstructed the pylorus and angulated the common duct.

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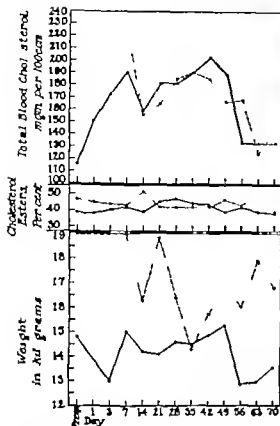


Fig. 1. Curves of average values. — Series I, partial obstruction of common bile duct. - - - Series II, partial obstruction of common bile duct. tib cholecystectomy.

normal limits, despite the observed rise and fall.

**Calcium.** The total blood serum calcium in the first series with only the obstruction showed a rise and then a fall. In the second series there occurred a slight steady rise the significance of which is questionable.

The literature has many conflicting reports on both the quality and quantity of the blood calcium in jaundice (Ivy 20). The presence of icterus has some effect on the metabolism of calcium as shown by the bony changes occurring in prolonged jaundice (Buchbinder and Kern 9) by the greater tolerance of the jaundiced dog to intravenous calcium (Walters and Bowler) and by the decreased effectiveness of parathyroid extract in parathyroidectomized dogs with jaundice (Buchbinder and Kern 10).



Fig. 2. The lower end of the common bile duct in dogs, showing the strictures produced. On the left the silver clip has ulcerated through only partially.

**Fibrin.** The fibrinogen content of the blood increased in both series. Snell, Greene and Rowntree (41) observed a sharp postoperative rise in blood fibrin after ligation of the common duct followed by a decrease to the upper limits of normal. The changes observed are in accord with the belief that damage to the liver causes a rise in blood fibrinogen and fibrin.

**Cholesterol and cholesterol esters.** The values for total blood cholesterol varied similarly in both series. There was a rise to a peak at the end of 7 days, a sharp fall at 14 days, a secondary rise between the thirty-fifth and forty-second day, with a final drop to the pre-operative level (Fig. 1).

The cholesterol esters, on the other hand, reacted conversely in the two series. In the series in which the obstruction was present alone the percentage of esters rose as the total cholesterol fell and fell when the total cholesterol rose. When the gall bladder was removed in addition to the presence of the partial obstruction, the changes in cholesterol esters paralleled the changes in total cholesterol (Fig. 1).

The significance of these changes is hard to evaluate. It is generally conceded that a rise in free cholesterol with a fall in the esters means liver damage (11, 14, 17, 23, 33, 37). In both the series of dogs one may postulate approximately an equal amount of ultimate liver damage. The difference, therefore, should be due to the presence of the gall bladder in the

TABLE I—BLOOD CHANGES FOLLOWING PARTIAL OBSTRUCTION TO COMMON BILE DUCT

Time Days	Weight kilos	Red blood cells Millions	Hemoglobin Gm/100 c.cm	Coagulation time Seconds	Cholesterol total Mg/100 c.cm	Cholesterol esters Per cent	Total calcium Mg/100 c.cm	Icteric index	Blood urea nitrogen Mg/100 c.cm	Fibrinogen Gm/100 c.cm
Pre-op	19 0	8 54	17 1	243	160	46 5	9 6	2 4	5 5	346
1		8 09	16 1	205	182	45 0	9 8	3 5	6 0	350
3		8 09	16 1	260	201	44 0	9 9	7 4	5 1	380
7	19 0	7 75	15 8	251	220	43 0	11 0	14 3	6 3	485
14	16 3	7 51	15 4	254	156	51 0	10 5	12 7	7 0	388
21	18 8	6 45	14 0	250	165	42 0	10 8	8 6	6 2	377
28	16 4	6 42	14 1	265	186	42 0	12 7	9 0	6 5	450
35	14 3	6 65	14 4	216	192	42 5	9 7	7 4		
42	15 7	6 79	13 9	42	185	42 5	9	7 4		
49	16 9	6 82	14 4	226	167	46 0	8 6	5 3		
56	16 0	6 23	13 4	214	168	43 5	8 3	5 5		
63	17 9	6 26	11 4	217	125	49 0	8 7	3 0		
70	16 8	6 55	14 0	201	144	39 0	9 3	2 7	10 0	

first series Sweet reported that after cholecystectomy the blood cholesterol rose and did not return to normal for 40 days. Previous experiments by many workers (1, 2, 4, 11, 12, 16, 18, 23, 31, 32, 33, 44) on the action of the gall bladder on cholesterol metabolism are contradictory, the best data appear to show that the normal gall-bladder mucosa may absorb small amounts of cholesterol, while the inflamed mucosa may add cholesterol to the gall-bladder bile by desquamation (Ivy, 19,

Tornoumi). The changes described would signify then, that the rise in total cholesterol is in response to liver damage, while the change in the esters is caused by an absorption of cholesterol from the bile with the amount of the esters in the blood remaining the same. This resulted in a relative drop in the cholesterol-cholesterol ester ratio. When the total cholesterol value dropped, the percentage of esters remained more or less the same, and the relative increase of esters became apparent.

TABLE II—BLOOD CHANGES FOLLOWING PARTIAL OBSTRUCTION TO COMMON BILE DUCT AFTER CHOLLECYSTECTOMY

Time Days	Weight kilos	Red blood cells Millions	Hemoglobin Gm/100 c.cm	Coagulation time Seconds	Cholesterol total Mg/100 c.cm	Cholesterol esters Per cent	Total calcium Mg/100 c.cm	Icteric index	Blood urea nitrogen Mg/100 c.cm	Fibrinogen Gm/100 c.cm
Pre-op	15 8	7 54	15 4	247	114	38 5	9 4	3 2	11 5	235
1		7 86	16 0	216	150	38 0	9 8	44 3	8 4	373
3	13 0	6 95	14 7	268	173	40 1	9 5	13 6	9 0	346
7	15 0	6 51	13 6	264	190	42 0	9 7	14 0	8 0	292
14	14 2	6 20	13 8	240	159	39 0	10 3	15 5	10 7	331
21	14 1	6 78	14 0	232	151	45 0	10 4	9 4	11 2	
28	14 6	6 82	14 0	220	181	47 0	10 3	6 4	10 7	420
35	14 5	6 11	13 4	250	190	44 5	9 9	7 2	8 55	
42	14 9	6 25	13 9	263	203	43 0	10 6	6 25	7 8	
49	15 3	6 37	13 4	228	189	39 0	10 1	5 6	8 5	410
56	12 0	6 40	11 6	256	134	42 0	9 6	12 "	1 0	
63	13 0	6 92	13 4	208	114	39 0	10 4	6 5	8 0	
70	13 6	6 61	13 2	33	134	35 5	10 1	5 0	8 5	

It has been shown that during fat absorption the proportion of cholesterol esters is high (Bloor and Knudson 7, 21 and Currie). Pathologically cholesterol deposits may be seen in any tissue in which cells are undergoing destruction and where absorption is poor (Wells). If these observations are accepted it is quite possible that the rise in the level of the esters is an absolute one caused by degeneration of the liver secondary to obstruction.

The secondary rise in total cholesterol coming between the fifth and sixth weeks may have been due to the liver damage becoming more apparent before the healing process began.

It was suggested that the variations in cholesterol and its esters may have been due to the nutritional state of the animals. These variations of the serum lipoids with the state of nutrition have been studied (Van and Glöden, and Wendt). In general, during starvation an initial hypocholesterolemia occurred after which the cholesterol values varied with the state of nutrition. In both series of observations reported here the initial drop in total cholesterol did not occur although there was a definite loss in weight. The total cholesterol rose until the seventh day. Thereafter in the dogs with the partial obstruction present and the gall bladder removed the two curves varied directly (Fig. 1). At the end of the period of observation, however when the cholesterol returned to normal, the weight had fallen appreciably. In the series of dogs with only the obstruction, after the initial rise in cholesterol, the two curves varied inversely, similar to the cholesterol-cholesterol ester curves in the same dogs. From these results it cannot be said that the changes in the blood cholesterol were caused by the variation in the state of nutrition.

It is more probable that the changes in the total cholesterol are the result of the liver damage.

At the end of the experiment the presence of partial obstruction was proved at autopsy. All the dogs showed strictures at the point where the clip had been placed (Fig. 2). The clips had ulcerated through and in 4 dogs it was found lying free in the upper common

duct. The bile back of the structure contained small sandy particles and was turbid. The liver was cirrhotic in all the dogs. The pancreas was normal. The duodenum and stomach showed gross inflammation only in 2 dogs.

#### SUMMARY

A study of the comparative effects of partial obstruction to the common bile duct with and without cholecystectomy was made (Tables I and II). It was hoped that some help might be obtained in explaining symptoms arising from partial or recurring common duct obstruction in man. The observations in the main agree with those noted after ligation of the common duct differing only in degree. A peculiar variation in the cholesterol-cholesterol ester ratio has been shown to occur. In the presence of obstruction and an intact gall bladder the cholesterol esters increased when the total cholesterol decreased, and decreased when the total cholesterol increased. In the presence of obstruction and with the gall bladder removed, the cholesterol esters varied directly with the total cholesterol. The evidence favors the view that these variations result from damage to the liver with the gall bladder playing a secondary rôle rather than from changes in the state of nutrition.

#### BIBLIOGRAPHY

1. YOC, DOW and GOMOREVITZ, MARIA. Cholesterols and Bileacids in the Gall and its diagnostic Wert. *Arch. f. Verdauungskr.* 937, 6, 337-343.
2. ANSCHUTZ, L. Zur Frage der Cholesterinbildung in der Gallenblase. *Münchener Med. Wochenschr.* 906, 33, 347-348.
3. ANSCHUTZ, L. and BACHMUTZ, A. Die Cholesterinase. *Jena. G. Fischer.* 909.
4. BAUMGARDT, F. A. and DALL, H. H. The obstructive mechanism of the gall bladder and its extrinsic nervous control. *J. Physiol.* 904-6, 33, 38-51.
5. BIERO, J. Studien über die Funktion der Gallenorgane unter normalen und gewissen abnormen Verhältnissen. *Acta chirurg. Scand.* 9, Suppl. 2: 1-15.
6. BERT, R. R. and HICKER, N. F. Biliary dyscrasia: physiological obstruction of the common bile duct. *Burg. Gynec. & Obst.* 935, 6, 7-734.
7. BLOOR, W. R. and KILBOURN, ARTHUR. Cholesterol and cholesterol esters in human blood. *J. Biol. Chem.* 9, 7, 89, 7-13.
8. BOULANGER, J. L., MAYER, F. C. and MAO TH T. S. Studies on the physiology of the liver VIII. Effect of total removal of the liver on the formation of urea. *Am. J. Physiol.* 924, 60, 57-72.
9. B. CHRISTENSEN, W. C. and KIRBY, RUTH. Blood calcium deficiency in experimental obstructive jaundice. *Am. J. Physiol.* 927, 80, 17-27.

tetanus toxins when injected subcutaneously into guinea pigs and white mice, do not give rise to tetanus but lie dormant as inert bodies at the point of injection, awaiting either destruction by phagocytes or an awakening into activity and toxin production by tissue destruction or secondary infection. It would, therefore, seem that the symptoms of tetanus which Babes observed in his animals were due to the amount of toxin that was injected with the bacilli in the cultures, and the important factor of toxin content was not controlled. It is quite plausible that the animals receiving a sublethal amount of tetanus toxin survived, while those receiving a fatal dose died. That he was able to save 1 of 2 animals inoculated with a culture of *Clostridium tetani* following the injection of the blood of a rat which had survived inoculations of *Clostridium tetani* and phenol may be explained on the basis that either the toxin injected was of a sublethal quantity, or that there was sufficient antitoxin in the blood of the rat to render the recipient animals passively immune. Of course, both factors may have played a part. In either event, it would be impossible to state that the phenol played any significant rôle.

McClintock and Hutchings performed some experiments similar to those of Babes. In their first experiment they used 5 pigs and gave each subcutaneously ten times the minimal fatal dose of U. S. standard tetanus toxin. As soon as symptoms developed the pigs were given 0.5 cubic centimeter of a 20 per cent phenol solution subcutaneously every 2 hours during the day. All of the pigs died and no effect was observed. They repeated this experiment and gave the phenol every 2 hours day and night. In this experiment 2 of the pigs recovered. They again repeated the experiment, the phenol injections being started immediately after the injection of the toxin. In this case all of the pigs died. Similar results were obtained in experiments on sheep. It did appear to them that the sheep were less spastic when treated with phenol than with antitoxin.

Camus, working with dogs, found phenol of no value in treating tetanus, regardless of the amounts used, or at what stage of the disease

the phenol was administered. He used tetanus toxin and a 30 per cent aqueous solution of phenol subcutaneously in varying amounts. The largest amount of phenol used was 20 cubic centimeters daily. The controls and the phenol injected dogs died in about the same time, i. e., 5 to 6 days. The dogs injected with phenol 24 hours after the administration of the toxin died at the same time as did the dogs which received the injections at the time the signs of generalized tetanus developed. Flores obtained similar results. He used 11 guinea pigs, giving each one a fatal dose of toxin intramuscularly, and at the first signs of tetanus administered a total of 3 cubic centimeters of a 10 per cent aqueous solution of phenol daily in fractional doses. Four of the guinea pigs died on the second day and the remainder on the third day. The 17 control animals died in 2 to 4 days, 14 of them on the third day.

It would seem from the 3 latter reports that the phenol treatment, as recommended by Baccelli, is of no benefit. However, there are many clinical reports of the cures of cases of tetanus with phenol injections, including a number of cases which had trismus and opisthotonos with generalized spasms. Most of the reports are based upon only 1 or 2 cases. Very few fatal cases have been reported in which this therapy was used. Baccelli, in 1911 (4), collected 190 cases from the literature from 1888 to 1911. These cases were from about one hundred different physicians. Baccelli divided the cases into groups. He classed 94 as severe, of which he stated 92 were cured, the mortality being decreased according to his calculation from 100 per cent to 2.12 per cent. He discarded from this group all cases which did not receive at least 1 gram of phenol per day. In the group that he classified as being very severe there were 38 cases, 11 of which, he stated, did not receive sufficient phenol. From the 27 cases that he thought did get sufficient phenol 22 were cured, a mortality, according to Baccelli, of 18.5 per cent. He stated that the average maximum dose was 1.5 grams of phenol per day, but often more was given. Single doses ranged from 0.1 to 0.15 gram. It was possible, however, to increase the dose in a 9 year old boy to 0.75



## THE EFFICACY OF PHENOL AND TETANUS ANTITOXIN IN THE TREATMENT OF EXPERIMENTAL TETANUS

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THE use of phenol in the treatment of tetanus antedates the isolation and culture of the *Clostridium tetani* by Kitasato in 1889 (15). Guakdi, a student of Baccelli, in 1888 reported before the First Italian Congress of Internal Medicine the excellent results obtained by him and Baccelli in the treatment of several hundred cases of neuralgia, sciatica, and other conditions by the injection of aqueous solutions of phenol. Finding the chemical to be a powerful analgesic and sedative, they were tempted to try it on a severe case of tetanus. The patient recovered. Baccelli became a staunch advocate of this type of treatment which has become identified with him to the extent that it commonly bears his name.

In his paper in 1911 Baccelli referred to the work of Kitasato (16) in 1891 and that of Babes (2) in 1892 as lending experimental support to the use of phenol in the treatment of tetanus. Kitasato discovered that phenol, when mixed with a filtrate from a culture of *Clostridium tetani*, *in vitro* would detoxify the toxin. He found that when equal amounts of a 3.0 per cent phenol solution and filtrate were combined and the mixture allowed to stand for one hour 0.1 cubic centimeter of this solution would not cause tetanus when injected into mice. It required only .00001 cubic centimeter of the filtrate itself to kill a mouse in 5 to 6 days. Baccelli failed to mention in his paper that Kitasato also found other chemicals to be of benefit in even lower concentration. For example, hydrochloric acid was effectual in 0.5 per cent solution, cresol in 1.0 per cent solution, calcium hypochloride in 0.1 per cent solution and sodium hydrosulfide in 0.3 per cent solution.

In referring to the work of Babes, Baccelli stated that this investigator found that he

could immunize animals to tetanus with the blood or serum of several species of animals which had been previously immunized by injections of phenol. This "experiment" consisted in taking blood from the heart of a rat which had survived *Clostridium tetani* and phenol injections, and injecting this into two guinea pigs. Both animals were then injected with a culture of the *Clostridium tetani*. One survived. He obtained the same results using rabbits.

In 1898 Babes (3) summarized his experiments, stating that he had cured dogs which had been inoculated with a virulent culture of *Clostridium tetani* by injecting them five times daily with 25 cubic centimeters of a 0.5 per cent solution of phenol, even when the treatment was delayed until first symptoms appeared. All the control animals died but all of the treated dogs recovered in about 9 days. Relaxation of muscle spasm appeared first at the point of the phenol injections. Pigeons were also used. 6 were inoculated with a culture of *Clostridium tetani*, and as soon as the first signs of the infection appeared, 3 were injected 8 times daily with 1 to 2 cubic centimeters of a 1.0 per cent solution of phenol. The treated animals survived while the 3 controls died. Similar results were obtained in rabbits but rats were rarely saved. The results in these experiments were much more constant than in similar experiments reported in 1892 in which he used a 1:1000 solution of phenol. In closing he said "The general result of this treatment is very remarkable and hardly less manifest than the action of antitetanic serum. The animals cured were not however absolutely immune to new tetanus inoculations but succumbed after repeated injections of toxin."

It does not appear that any definite conclusions can be drawn from these experiments for Francis and Vaillard and Rouget found that tetanus spores in pure culture and free from

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Voled by grant from the Eli Lilly Company



Fig 1 Dog 418, cord Received 100 D.L.D. of tetanus toxin (pulverized) intravenously Sacrificed at 25 hours when near death Anterior horn cells show acute cell dis ease with loss of Nissl substance and pale staining of cell prolongations far from the cell The nuclear membrane is lost a, left,  $\times 500$ , cresyl violet stain b,  $\times 400$ , cresyl violet stain

treatment, and we have found no Italian report on wartime tetanus which mentions the Baccelli method Corniglion stated that the French Army had been using phenol successfully both in prophylaxis and treatment but no mention was made of the dosage He reported 4 patients who recovered after the administration once daily by either intramuscular or intravenous routes of 40 to 70 cubic centimeters of a 10 per cent aqueous phenol solution It was, perhaps, as the result of war experiences that little appeared in the literature until 1931 when Suvansa published a report of 14 cases with only 4 deaths Of the 4 that died 3 were moribund upon admission and 1 died from uremia These results, compared with the poor results he had been getting with antitoxin therapy, led him strongly to advise its use He administered intrathecally a 1.400 solution of phenol in normal saline in dosage of 30 to 40 cubic centimeters to adults and 12 to 20 cubic centimeters to children Since the publication of this article he has had 12 additional cases (23) with 5 deaths and 7 recoveries from 1931 to 1934 However, from 1934 to the present time he has been able to obtain a larger supply of antitoxin and has used it with fairly good results, injecting 60,000 to 120,000 international units sub-



Fig 2 Dog 382, cerebrum Received 0.57 cubic centimeter of phenol (1.400) per kilogram of body weight intrathecally and was sacrificed at 72 hours Thickening and edema of the meninges over the cortex  $\times 110$ , hematoxylin and eosin stain

cutaneously daily He is still of the opinion that phenol can cure those conditions which are not too severe He uses the pulse rate as a standard of severity Patients who have a pulse rate of over 100 in adults or 120 in children (the pulse rate being taken between the spasms) he considers to have "severe" conditions He further stated that tetanus resulting from wounds of the head and the neck is not amenable to phenol treatment At the same time Piloni reported the results of 53 cases of tetanus observed during the 12 previous years treated with phenol alone Of the cases which had an incubation period of 3 days or less all died, from 3 to 10 days 6 died and 8 survived, from 10 to 30 days, only 1 died out of 28 His maximum dose per day was 0.85 gram given subcutaneously in fractional doses, following the technique of Baccelli He used no tetanus antitoxin

TABLE I.—RESULTS OF EXPERIMENTS WITH SUVANSI METHOD

No.	Weight Kilo	Tetanus toxin 100 D.L.D. M.C.D.	Tetanus infection			Phenol dose 57 cc./kg intracutaneously		Death from tetanus No. hours after onset	Remarks
			Unit I.V.†	Neutral ising cherry Ureth.	Time interval after local I.V. hrs.	cc.	% hours after onset		
405		100,000 oil						44½	Onset of ascending tetanus in 25 hours
414		200,000 oil						48	Onset of ascending tetanus in 26 hours
	8	470,000 poly							Descending tetanus
416	8	260,000 poly						26	Onset of descending tetanus about 6 hours
417		30,000 poly						25	Onset of descending tetanus in 19 hours
417	8	470,000 poly						26	Onset of descending tetanus in 29 hours
418									Shed weakness right leg for few hours. Day 21 U.L. 4 days later
	6					6.04			Right weakness left leg for 4 days. Otherwise U.L.
419	8.6								No signs.
420		275,000 oil				3.06			Onset of ascending tetanus in 10 hours
	6.5	200,000 poly				11	6		Ascending tetanus
421		215,000 poly					6	20.1	Descending tetanus
422		460,000 oil				3	56	21	Onset of ascending tetanus in 24 hours
427		23,000 oil	84.00	100					Dead from dysentery 7 days later. No tetanus
428		4,000 oil	8.300	100	6				Developed local tetanus at site of toxin injection 30 hours later. Never generalized tetanus
429	9	50,000 poly	94.000	100					Dead in 26 hours of severe unrelieved dysentery
430		41,000 oil	84.700	100			26		Dead from dysentery 4 days later. No tetanus.
441	8	35,000 oil	30.00	100	6	27			Dead from dysentery 3 days later. No tetanus
442	8.7	50,000 oil	83.000	100		4.27			Dead from dysentery 3 days later. No tetanus

\* 1 day local dose equals 30 minimum local doses per kilogram.

† unit intracutaneous 1000 M.C.D.

gram every 12 hours, for 12 days. Other patients were given as much as 3.0 grams per day for 14 days without apparent harm. He himself used a 2.0 to 3.0 per cent aqueous solution and gave not more than 0.3 to 0.5 gram the first day but if the urine remained normal, he quickly increased the dose from 1.0 to 1.5 grams per day in divided doses. Woods used a 10 per cent solution and Maragliano used a 5 per cent solution in sterile oil to avoid the local effects of phenol especially in new born babies. In the very severe cases, Baccelli advised the immediate injection of 1 gram the first day.

As a result of Baccelli's paper there was from 1911 to 1914 a gradual increase in the publications of isolated cases of tetanus cured by phenol. However from 1914 on the reported cases became rarer. Bruce in 1915 (7)

and 1916 (8) stated that magnesium sulphate and phenol had been used in the cases of tetanus in the home hospitals of England but had been found to be of no value. In the first report 7 patients died of those receiving subcutaneous doses of less than 16.2 grams of phenol per day and 5 recovered, while of those receiving from 16.2 to 80.0 grams per day 7 died and 6 recovered. In the second report about the same ratio prevailed. All of these patients also received tetanus antitoxin. Leishman and Smallman, in their analysis of the cases of tetanus in the British Expeditionary Forces in France, reported no favorable results from the use of phenol. However they reported neither the amount of phenol used nor the method of administration. Stricker writing on tetanus in Germany during the war made no mention of the phenol



Fig 1 Dog 418, cord Received 100 D L D of tetanus toxin (pulverized) intravenously Sacrificed at 25 hours when near death Anterior horn cells show acute cell disease with loss of Nissl substance and pale staining of cell prolongations far from the cell The nuclear membrane is lost a, left,  $\times 500$ , cresyl violet stain b,  $\times 400$ , cresyl violet stain

treatment, and we have found no Italian report on wartime tetanus which mentions the Baccelli method Corniglion stated that the French Army had been using phenol successfully both in prophylaxis and treatment but no mention was made of the dosage He reported 4 patients who recovered after the administration once daily by either intramuscular or intravenous routes of 40 to 70 cubic centimeters of a 10 per cent aqueous phenol solution It was, perhaps, as the result of war experiences that little appeared in the literature until 1931 when Suvansa published a report of 14 cases with only 4 deaths Of the 4 that died 3 were moribund upon admission and 1 died from uremia These results, compared with the poor results he had been getting with antitoxin therapy, led him strongly to advise its use He administered intrathecally a 1.400 solution of phenol in normal saline in dosage of 30 to 40 cubic centimeters to adults and 12 to 20 cubic centimeters to children Since the publication of this article he has had 12 additional cases (23) with 5 deaths and 7 recoveries from 1931 to 1934 However, from 1934 to the present time he has been able to obtain a larger supply of antitoxin and has used it with fairly good results, injecting 60,000 to 120,000 international units sub-



Fig 2 Dog 382, cerebrum Received 0.57 cubic centimeter of phenol (1.400) per kilogram of body weight intrathecally and was sacrificed at 72 hours Thickening and edema of the meninges over the cortex  $\times 110$ , hematoxylin and eosin stain

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Fig. 3. Dog 450, cord. Received 0.01 D.L.D. of tetanus toxin (solution) intravenously and 6 hours later .57 cubic centimeter of phenol (.400) per kilogram of body weight intrathecally. Dog died in 3 hours from tetanus. Anterior horn cells in toxic disease. Chromatin diffusely stained. Nuclei barely visible. One cell shows encrustation of pericellular glia network.  $\times 440$ , hematoxylin and eosin stain.

Three American authors reported favorable results following phenol and antitoxin treatment. Bryan reported 6 cases with 6 recoveries. He used the phenol intravenously in a 10 per cent solution giving from 30 to 40 cubic centimeters every 8 hours. In addition, these patients received from 65,000 to 105,000 units of tetanus antitoxin. Bates reported 4 recoveries out of 5 cases following Baccelli's technique while Miller reported 1 successful case following the method used by Suvansa. Both of these authors also gave large doses of tetanus antitoxin in addition to the phenol. Prior to these reports, Beall in 1924 reported 8 successfully treated cases using 1 to 2 grains of phenol intramuscularly every 4 hours usually in a 150 per cent aqueous solution. In addition his patients received 30,000 units

of tetanus antitoxin on the first day. They all had trismus and convulsions. The incubation periods were reported in 5 cases and ranged from 2 to 12 days.

In many of these cases the tetanus antitoxin alone might have effected a cure regardless of the amount of phenol given yet it is not possible to state that the phenol did not supplement the antitoxin.

What can we conclude from these reported clinical successes? A patient will not succumb to tetanus unless he gets a full lethal dose of the toxin but just what a lethal dose is for man we do not know. There is no doubt that it will vary with the individual due to difference in host resistance. Furthermore, there is no test by which we can tell just how much toxin the patient has fixed or will absorb. Following the clinical course of the disease may help but little because we never know the exact incubation period, the number or virulence of the *Clostridium tetani* or their rate of toxin production. If we knew these facts we could then better prognosticate in the individual case. Even though it is theoretically possible for a patient to absorb and fix seven-eighths of a fatal dose of toxin and not die it is hardly possible to believe that all of the cases reported as having been cured by phenol alone would fall into this group. Because of the great expense involved in the treatment of tetanus with adequate amounts of tetanus antitoxin we felt that it would be of importance to carry out some controlled experiments in an attempt to determine the value of phenol in the treatment of experimental tetanus alone and in combination with antitoxin.

#### PART I

**Method.** We first investigated the method advocated by Suvansa (23). We assumed that he would use his maximum dose of 40 cubic centimeters in treating a young well developed man of 150 pounds with a severe case of tetanus. From this we obtained our intrathecal dose of 0.57 cubic centimeter per kilogram of body weight of a 1:400 phenol solution in normal saline. We desired to use a dose of tetanus toxin that we knew would kill the dog, regardless of the amount of tetanus



Fig 4 Dog 594, cord Received 100 D L D of tetanus toxin (pulverized) intravenously and 6 hours later 0.57 cubic centimeter phenol (1.400) per kilogram of body weight intrathecally Dog died in 20½ hours from tetanus Acute cell disease in anterior horn cell with loss of Nissl

substance, pyknosis of nucleus and swelling of nucleolus a,  $\times 840$  cresyl violet stain b, Thrombosis and liquefaction of gray matter around it  $\times 105$  c, Incrustation of pericellular glia network around degenerated anterior horn cells  $\times 840$

antitoxin administered Abel and Chalian had found that if 100 D L D<sup>1</sup> of tetanus toxin were injected intravenously and 6 hours allowed to elapse, no amount of tetanus antitoxin could save the animal We, therefore, decided to use this amount, since we felt that by so doing we could tell whether phenol was of any benefit in extreme tetanus, either alone or in combination with tetanus antitoxin

*Experimental data* Healthy, young, adult dogs were used for each group of experiments A complete autopsy was performed on each animal that died or was sacrificed

*Experiment 1* (1) The length of time required for dogs to die after the intravenous administration of 100 D L D of tetanus toxin was determined The symptomatology was carefully observed in the 6 dogs as tetanus developed (2) The effects of intrathecally

administered phenol (1.400) given in the dosage of 0.57 cubic centimeter per kilogram of body weight were studied in 3 dogs to which no toxin was given (3) Three dogs were given intravenously 100 D L D of tetanus toxin, and at the end of 6 hours were given intrathecal injections of phenol (1.400) in the same dosage as stated The progress of the disease and the length of time that the dogs survived were noted (4) Three dogs were prepared as in the third group, but instead of intrathecal phenol they were given at the end of 6 hours 200 times the neutralizing dose<sup>2</sup> of tetanus antitoxin intravenously and the subsequent course observed (5) In 1 dog we combined the above 2 forms of therapy so that at the end of 6 hours the dog, which had received 100 D L D of tetanus toxin, was given both intrathecal phenol as in No. 3, and 200 times the neutralizing dose of tetanus anti-

<sup>1</sup>From Abel and Chalian We have found in the course of very numerous experiments extending over a period of 5 years that injection of 450 guinea pig L D 50's per kilogram invariably induces fatal tetanus in dogs of medium weight and age, and have therefore arbitrarily chosen this figure as our lethal dose for dogs This dose kills dogs at random in from five to nine days

<sup>2</sup>According to the United States Government standard one unit of tetanus antitoxin will neutralize 1000 minimal lethal doses of tetanus toxin Therefore 200 times the neutralizing dose would be 200 times the amount of tetanus antitoxin which would be necessary to neutralize the total injection of the tetanus toxin

toxin as in No. 4. All of our intrathecal administrations were made through the lumbar route with a regular spinal puncture needle while the dogs were under ether anesthesia.

This series of experiments (Table I) revealed that dogs given 100 D.L.D. of tetanus toxin invariably died in 25 to 26 hours when the freshly prepared dry toxin was used, and in 42 to 44 hours when the toxin in solutions (of equal strength when prepared sometime prior to the experiment) was used. Histological study of the central nervous system revealed the toxic myelopathy so often described in tetanus (Fig. 1) while that of the kidneys revealed a simple nephrosis with passive congestion, the liver an acute passive congestion with parenchymatous degeneration most marked in the central zones. Dogs given phenol alone intrathecally showed no clinical effects, but the histological study of the cord and brain after the phenol was injected revealed a thickening of the meninges (Fig. 2) the kidney a mild simple nephrosis, and the liver a mild cloudy swelling. The dogs given tetanus toxin intravenously plus phenol intrathecally died about 5 hours sooner than the controls. Histological study of the central nervous system here revealed a toxic myelopathy greater than that observed with tetanus toxin (Figs. 3 and 4). However the kidney and liver showed much the same pathological picture as that found with toxin alone. The dogs which were given 100 D.L.D. of tetanus toxin and then after 6 hours treated with 200 neutralizing doses of tetanus antitoxin did not die of tetanus as predicted by Abel and Chailan. One dog survived and showed no ill effect whatsoever from the tetanus toxin and was in excellent condition when returned to stock 1 month later. Another dog developed local tetanus in the injected hind limb and was sacrificed at the end of 11 days. It at no time showed any signs of generalized tetanus. The remainder of the dogs died from intercurrent infection yet all but one lived sufficiently long after tetanus was expected to develop to preclude its subsequent development.<sup>1</sup> In the last

phase only 1 dog was given similar amounts of tetanus toxin and then treated at the end of 6 hours with both phenol and tetanus antitoxin. As would be expected from the above it also showed no signs of tetanus, but died from an intercurrent infection yet sufficiently long after the experiment was started similarly to preclude any development of tetanus. None of these dogs showed any of the neurological involvement seen in tetanus.

These experiments demonstrated that dogs given overwhelming doses of tetanus toxin known to kill healthy dogs in from 24 to 26 hours, are not helped. If anything their death is hastened by additional central nervous system damage or lowered resistance to distemper when given phenol intrathecally 6 hours after the tetanus toxin is given intravenously while the use of tetanus antitoxin alone in sufficient amounts can save the dogs when given 6 hours after the toxin.

*Experiment 2* In this group of dogs, we administered the same dosage of tetanus toxin and phenol as in the first experiment, but instead of waiting 6 hours to inject the phenol we administered it as soon as possible after the toxin injection. The results both as to the length of time before death from tetanus and to the histological findings, were similar to the findings in the first experiment.

## PART II

We felt that the above experiments revealed that phenol administered intrathecally in the amounts used was of no value in neutralizing or detoxifying large doses of tetanus toxin given intravenously to dogs, regardless of the time of administration. We, therefore began our investigation of the intravenous use of phenol as advocated by Corniglion and Bryan.

*Method* These authors have found clinically that fairly large amounts of a 10 per cent phenol solution were compatible with life. We, therefore adopted this percentage. Our solution was made by adding the required amount of liquid phenol of a known concentration to normal saline just prior to its use

<sup>1</sup>Under similar circumstances, we have found that if the dogs did not show signs of tetanus within 48 hours, they would not subsequently develop them. It, therefore, seemed all dogs that lived 48 hours or more from tetanus, although they may have succumbed at that time or later from another infection. The first signs of distemper noted were paralysis, dis-

charges from the nose and eyes. These were followed by cough, loss of appetite and general debility. On the dogs that died or were sacrificed, varying degrees of pulmonary congestion were found at postmortem. These changes ranged from simple bronchitis with pulmonary congestion to abscess or lobular pneumonia with abscess formation.







Fig. 5. Dog 936, cord. Received unpreserved tetanus antitoxin intrathecally and as sacrificed 17 hours. Mild lymphocytic infiltration in the arachnoid around an anterior horn rootlet.  $\times 205$ , cresyl violet stain.

normal position in which they were placed. Within 6 to 8 hours marked conjunctival edema was noted which in some cases resulted in a complete obliteration of the pupil. In the animals which received lethal doses of phenol these signs were progressive until death, while in the others the signs were less severe and entirely disappeared within 24 hours. Histological examination of the sections taken from the kidneys and livers revealed a simple nephrosis and mild cloudy swelling. These findings were, of course most marked in the dogs receiving the larger amounts of phenol. We concluded that in dogs the lethal dose of 1.0 per cent intravenous phenol was between 0.3 and 0.35 gram per kilogram of body weight, and that the damage to the kidney and liver was in direct proportion to the amount of phenol given.

**Experiment 2.** The purpose of these experiments was to determine whether or not the intravenous injection of phenol in one hind limb would prevent or prolong the appearance of tetanus when 100 D.L.D. of tetanus toxin

was simultaneously injected into the vein of the other hind limb. Because of the known damaging effects of both tetanus toxin and phenol we decided to use a dosage of phenol which in itself had minimal effects. Bio-assays were run on the bloods from all the dogs. The blood samples were taken in each instance at the conclusion of the injections. There were 3 dogs in this group (Table II) one control and two dogs receiving both phenol (0.107 and 0.143 gram per kilogram of body weight respectively) and tetanus toxin. All three of these animals died between 26 and 30 hours and all of the bio-assay determinations were found to be equal. Histological changes in the kidneys and liver were about the same as in the preceding experiment. We therefore concluded that intravenous 1.0 per cent phenol in the dosage mentioned, given simultaneously with 100 D.L.D. of tetanus toxin through opposite veins in the same fluid volume did not alter the progress of tetanus and the bio-assays did not reveal any detoxifying effect of the phenol.

**Experiment 3.** Although the above experiments were negative we decided to repeat them but using only 10 D.L.D. of tetanus toxin. In this series we had 2 controls and 6 experimental dogs (Table II) which received, respectively in addition to the toxin, 0.117, 0.117, 0.125, 0.222, 0.30 and 0.35 gram of phenol per kilogram of body weight. The controls died of tetanus in from 46 to 68 hours. The phenol dogs died of tetanus in from 46 to 66 hours with the exception of the last dog that received 0.35 gram of phenol per kilogram of body weight. This dog died in about 20 hours from phenol poisoning. The bio-assays in all the animals remained equal except in the 2 dogs which received larger amounts of phenol, and in these the bio-assays showed their blood to be more toxic for guinea pigs than that of the controls. It was noted in experiment 1 that in a normal dog the maximum tolerance was between 0.3 and 0.35 gram of phenol per kilogram of body weight. During this series it was found that the time of death of the last animal was approximately the same as that of the dog which received 0.35 gram of phenol

The authors are deeply indebted to Dr. F. O. Jones of the Biological Department of the Lilly Research Laboratories for his co-operation in making the blood samples.



TABLE III—RESULTS OF NEUTRALIZING DOSES OF TETANUS ANTITOXIN

Dog No.	Weight Kilo	Tetanus toxin 100 D.L.D. M.L.D.	Tetanus antitoxin		Death from tetanus	Remarks
			Units I.V.† hours after toxin	Neutralizing dose Unit	No. hours after toxin	
849	8	25,000 pulv	9600	5	24	Tetanus descending
850		25,000 pulv	1,0000	50	60	Tetanus descending
964		25,000 pulv	22,500	50	36	Tetanus descending
81	7	11,000 pulv	11,100	200		Tetanus descending
82		25,000 pulv	8,800	20	77	Tetanus descending
807	8	20,000 pulv	7,000		51	Tetanus descending
896	9	22,000 pulv	7,700	1	No tetanus	Returned to stock month later
897		22,000 sol	86,100		No tetanus	Died day later of distemper
498		25,000 sol	6,300		No tetanus	Developed local tetanus site of toxin injection. Killed day after toxin given
499	5	25,000 pulv	61,000		No tetanus	Died in 66 hours of distemper
	8	200,000 pulv	hours after toxin 249,000			Developed stiffness hind limbs and back 3rd day. No further advancement. Sacrificed 5th day because of anorexia and loss
21	8	61,000 pulv	5,100		144	Developed stiffness hind limbs and back 3rd day. Anorexia, etc. No further advancement. Signs seemed to be improving when found dead 5th day
17		2,000 pulv	8,100			Developed stiffness hind limbs and back 3rd day. No further advancement. Complete recovery

1 cc tetanus toxin = 1 M.L.D.

† 1 D.L.D. equals 100 M.L.D./Kg

toxin, we injected a group of 25 with this amount of toxin and after 6 hours intravenously various neutralizing doses of tetanus antitoxin (Table III). It was found that the time of death of these animals was almost in direct proportion to the amount of antitoxin administered e.g. the dog which received 25 times the neutralizing dose of antitoxin died from tetanus in 36 hours, while the animal that received 150 times the neutralizing dose died in 77 hours. Of the 2 animals which received 200 times the neutralizing dose, 1 died in about 51 hours, while the other had no evidence of tetanus and was returned to stock 1 month later in perfect condition.

These data with those in Part I experiment 1 led us to conclude that dogs given 100 D.L.D. of tetanus toxin could be saved if between 182 and 200 times the neutralizing dose was given.

Experiment 2 Since it had been found that dogs given 100 D.L.D. of tetanus toxin intrave-

nously had not irreversibly fixed one lethal dose of toxin within 6 hours, we decided to prolong the waiting period to 7 hours. Similarly we also increased the dosage of tetanus antitoxin from 200 times the neutralizing dose to 300 times, because our experience in the past has shown that the dosage of antitoxin must be proportionately increased with the time interval if the animal is to be saved. To 3 dogs, therefore we gave 100 D.L.D. of tetanus toxin intravenously and at 7 hours gave in a similar manner 300 times the neutralizing dose of tetanus antitoxin. The course of these animals was uneventful until the third day when all 3 developed stiffness of the back and hind limbs (ascending tetanus was not uncommon in our experience). In 2 of the animals the signs did not progress, however in 1 opisthotonos with inability to stand developed on the fourth day. The signs in this last dog remained stationary after the fourth day and seemed to be improving, but the animal was found dead on the morning of the sixth day. Of the 2 other dogs, 1 developed distemper

and was sacrificed on the fourteenth day because of its poor condition. The remaining dog gradually lost the spasticity and was in excellent condition when sacrificed 3 months later. Histological examinations of the kidney and liver were normal. There was, however, considerable thickening of the dura with mild infiltration of arachnoid, but the anterior horn and cortical cells appeared to be normal.

We concluded from these experiments that dogs can frequently be saved when 300 times the neutralizing dose of tetanus antitoxin is administered intravenously 7 hours after the intravenous injection of 100 D L D of tetanus toxin, although signs of tetanus may develop. We must assume that some of the toxin was so fixed within 7 hours that 300 times the neutralizing dose of antitoxin could not inactivate it. The histological study of the surviving animal which was sacrificed 3 months later revealed that most of the pathological changes induced by tetanus toxin were reversible.

#### SUMMARY AND CONCLUSIONS

1. Intrathecal administration of phenol to dogs given intravenously 100 D L D of a tetanus toxin known to kill healthy dogs within 25 to 26 hours, will not prevent death of the animals. If anything, their death is hastened by the additional central nervous system damage or lowered resistance to distemper which phenol apparently produces. The administration of tetanus antitoxin in sufficient amounts does save the dogs when given within 6 hours of a similar dose of toxin.

2. The lethal dose of a 10 per cent phenol solution for dogs was found to lie between 0.3 and 0.35 gram per kilogram of body weight when given intravenously. The damage to the kidneys and livers was in direct proportion to the amount of phenol given.

3. Intravenous 10 per cent phenol in the dosage used, given simultaneously with 100 D L D of tetanus toxin through opposite veins, did not alter the progress of the tetanus and the bio-assays did not reveal any detoxifying effect of the phenol.

4. Intravenous 10 per cent phenol in the dosage used, given simultaneously with 10 D L D of tetanus toxin through opposite veins, did not alter the progress of the tetanus

and bio-assays did not reveal any detoxifying effect of the phenol.

5. The common preservatives used in tetanus antitoxin are definite irritants to the central nervous system. Tetanus antitoxin containing these preservatives should not be used athetically in the treatment of tetanus.

6. Dogs given 100 D L D of tetanus toxin intravenously were saved when given at 6 hours between 182 and 200 times the neutralizing dose of tetanus antitoxin.

7. Dogs given 100 D L D of tetanus toxin intravenously were saved when given at 7 hours 182 times the neutralizing dose of tetanus antitoxin, although signs of tetanus developed. It was suggested that in 7 hours a portion of the injected tetanus toxin was so irreversibly fixed that it could not be neutralized by dosage of antitoxin given.

The authors wish to express their appreciation to Dr F H L Dr Harold M Dixon for their help in the study of biological specimens and to Dr I S Ravdin and Lockwood for their encouragement and counsel.

#### BIBLIOGRAPHY

- 1 AB and CHALIAN, W Bull Johns Hopkins, 62, 610
- 2 BA n de l'Institut de Path et de Bact. de 92-1893, 5, 361
- 3 Ide Century Practice of Medicine, 1898,
- 4 BA Berl klin Wchnschr, 1911, 1, 1021
- 5 BA Am J Surg, 1932, 18, 58
- 6 BE Texas State J M, 1924, 20, 54
- 7 BR acet, 1915, 2, 901
- 8 Ibi 29
- 9 BR Tenn M Ass, 1933, 26, 242
- 10 CAJ oc de biol, Paris, 1912, 72, 109
- 11 CO de med et chir prat, 1915, 86, 449
- 12 FL pt rend Soc de biol, 1920, 83
- 13 FR U S Hyg, Lab, No 95, 1914
- 14 GU by Deplano, G G Gaz d osp,
- 15 KIT chr f Hyg u Infektionskrankh
- 16 Ibi 25
- 17 LEI nd SMALLMAN, A B J Roy Army
- 18 MA 7, 28, 295
- 19 MC ted by Baccelli, loc cit
- 20 I, and HUTCHINGS, W H J
- 21 MIL 13, 309
- 22 PIL nsas M Soc, 1933, 34, 436
- 23 STRI, 1931, 38, 510
- 24 I che med Wchnschr, 1919, 45
- 25 SUV 1931, 1, 1075
- 26 Ide unication
- 27 VAI GET J Ann de l'inst Pasteur,
- 28 18
- 29 Woo ccelli, loc cit.

TABLE III—RESULTS OF NEUTRALIZING DOSES OF TETANUS ANTITOXIN

Dog No.	Weight lbs.	Tetanus toxin 100 D.L.D. M.L.D.	Tetanus antitoxin		Death from tetanus	Remarks
			Units I.V.†	Neutralizing doses Units	Hours after toxin	
1	8	36,000 units	9000	25	38	Tetanus descending
870	10	36000 units	22000	30	40	Tetanus descending
90		26000 units	26000	300	90	Tetanus descending
82		25 1000 units	5500	100	75	Tetanus descending
		21000 units	120	50	37	Tetanus descending
		30000 units	2000	5	55	Tetanus descending
877	8	30000 units	7870	No tetanus		Returned to stock month later
886		30000 units	40000	No tetanus		Dead days later of distemper
477		43000 units	40000	No tetanus		Developed local tetanus side of toxin injection killed days after local ptosis
440		43000 units	8700	No tetanus		Dead in 60 hours of distemper
39	8	36000 units	100	No tetanus		
314	8	36000 units	7 hours after toxin (10000)			Developed stiffness hind limbs and back 3rd day. No further advancement. Died 1st day because of subcutaneous infection
		44,000 units	54,000		24	Developed stiffness hind limbs and back 3rd day. Apoptosis of No further advancement. Seem to be improving when killed 4th day
21	8	44,000 units	54,000			Developed stiffness hind limbs and back 3rd day. No further advancement. Complete recovery

† D.L.D. equals 100 M.L.D./Kg

correlates with M.L.D.

toxin we injected a group of 4 with this amount of toxin and after 6 hours intravenously various neutralizing doses of tetanus antitoxin (Table III). It was found that the time of death of these animals was in direct proportion to the amount of antitoxin administered e.g. the dog which received 25 times the neutralizing dose of antitoxin died from tetanus in 38 hours, while the animal that received 100 times the neutralizing dose died in 77 hours. Of the 3 animals which received 100 times the first times the neutralizing dose, 1 in about 153 hours, while the other 2 had no evidence of tetanus and was returned to stock 1 month later in perfect condition.

These data with those in Part I experiment 1 led us to conclude that dogs given 100 D.L.D. of tetanus toxin could be saved if between 182 and 200 times the neutralizing dose was given at once.

Experiment 2 Since it was found that dogs given 100 D.L.D. of tetanus toxin intra-

venously had not irreversibly fixed one lethal dose of toxin within 6 hours we decided to prolong the waiting period to 7 hours. Similarly we also increased the dosage of tetanus antitoxin from 300 times the neutralizing dose to 500 times, because our experience in the past has shown that the dosage of antitoxin must be proportionately increased with the time interval if the animal is to be saved. To 3 dogs therefore we gave 100 D.L.D. of tetanus toxin intravenously and at 7 hours gave in a similar manner 500 times the neutralizing dose of tetanus antitoxin. The course of these animals was uneventful until the third day, when all 3 developed stiffness of the back and hind limbs (ascending tetanus was not uncommon in our experience). In 2 of the animals the signs did not progress, however in 1 opisthotonos with inability to stand developed on the fourth day. The signs in this last dog remained stationary after the fourth day and seemed to be improving but the animal was found dead on the morning of the sixth day. Of the 2 other dogs 1 developed distemper

and was sacrificed on the fourteenth day because of its poor condition. The remaining dog gradually lost the spasticity and was in excellent condition when sacrificed 3 months later. Histological examinations of the kidney and liver were normal. There was, however, considerable thickening of the dura with mild infiltration of arachnoid, but the anterior horn and cortical cells appeared to be normal. We concluded from these experiments that dogs can frequently be saved when 300 times the neutralizing dose of tetanus antitoxin is administered intravenously 7 hours after the intravenous injection of 100 DLD of tetanus toxin, although signs of tetanus may develop. We must assume that some of the toxin was so fixed within 7 hours that 300 times the neutralizing dose of antitoxin could not inactivate it. The histological study of the surviving animal which was sacrificed 3 months later revealed that most of the pathological changes induced by tetanus toxin were reversible.

#### SUMMARY AND CONCLUSIONS

- 1 Intrathecal administration of phenol to dogs given intravenously 100 DLD of a tetanus toxin known to kill healthy dogs within 25 to 26 hours, will not prevent death of the animals. If anything, their death is hastened by the additional central nervous system damage or lowered resistance to disorder which phenol apparently produces. The administration of tetanus antitoxin in sufficient amounts does save the dogs when given within 6 hours of a similar dose of toxin.
- 2 The lethal dose of a 10 per cent phenol solution for dogs was found to lie between 0.3 and 0.35 gram per kilogram of body weight when given intravenously. The damage to the kidneys and livers was in direct proportion to the amount of phenol given.
- 3 Intravenous 10 per cent phenol in the dosage used, given simultaneously with 100 DLD of tetanus toxin through opposite veins, did not alter the progress of the tetanus and the bio assays did not reveal any detoxifying effect of the phenol.
- 4 Intravenous 10 per cent phenol in the dosage used given simultaneously with 10 DLD of tetanus toxin through opposite veins, did not alter the progress of the tetanus

and the bio-assays did not reveal any detoxifying effect of the phenol.

- 5 The common preservatives used in tetanus antitoxin are definite irritants to the central nervous system. Tetanus antitoxin containing these preservatives should not be used intrathecally in the treatment of tetanus.
- 6 Dogs given 100 DLD of tetanus toxin intravenously were saved when given at 6 hours between 182 and 200 times the neutralizing dose of tetanus antitoxin.
- 7 Dogs given 100 DLD of tetanus toxin intravenously were saved when given at 7 hours 30 times the neutralizing dose of tetanus antitoxin, although signs of tetanus developed. It was suggested that in 7 hours a portion of the injected tetanus toxin was so irreversibly fixed that it could not be neutralized by the dosage of antitoxin given.

The authors wish to express their appreciation to Dr F H Lewis, Dr Harold M Dixon for their help in the study of our pathological specimens and to Dr I S Ravin and Dr J S Lockwood for their encouragement and counsel so wisely given.

#### BIBLIOGRAPHY

- 1 ABEL J J, and CHALIAN W. Bull Johns Hopkins Hosp, 1935, 6: 110.
- 2 BABES V. Ann de l'Institut de Path et de Bact de Bucarest, 18, 1896, 361.
- 3 Idem. 20th Century Practice of Medicine, 1898, 17: 119.
- 4 BACCILLI G. Berl Klin Wchnschr, 1911, 1: 1021.
- 5 BATES C O. Am J Surg, 1932, 18: 58.
- 6 BEALL K H. Texa State J M, 1924, 20: 54.
- 7 BRUCE D. Lancet, 1901, 901.
- 8 Ibid, 1916, 29: 9.
- 9 BRYAN W A. J Intern M Ass, 1933, 26: 242.
- 10 CAMUS C. R Soc de Biol Paris, 1912, 72: 109.
- 11 CORNILLON J. J de med et chir prat, 1915, 86: 449.
- 12 FLORES P. Compt rend Soc de biol, 1920, 83: 907.
- 13 FRANCIS E. Bull U S Hyg Lab No 95, 1914.
- 14 GUALDI. Quoted by Decker C. G. Gaz d osp, 1903, 4: 8, 8.
- 15 KITASATO S. Ztschr f Hyg u Infektionskrankh, Leipz, 1899, 7: 225.
- 16 Ibid, 1901, 10: 120.
- 17 LEISHMAN W B, and SYMES A. A B J Roy Army Med Corps, 1911, 1: 1.
- 18 MARAGLIANO. Quoted by Decker C. G. J Hyg, 1913, 13: 1.
- 19 MCCLINTOCK, C. F. J Hyg, 1913, 13: 1.
- 20 MILLER I S. J Clin M, 1933, 34: 436.
- 21 PILLONI S. Polyclin, 1909, 1069.
- 22 STRICKER I. Deutsch Wchnschr, 1919, 45: 1069.
- 23 SUYANSA S. Lancet, 1919, 1: 1.
- 24 Idem. Personal communication.
- 25 VILLARD, L., and ROUILLON. J Hyg, 1892, 8: 385.
- 26 WOODS. Quoted by Baccilli.

# ECLAMPSIA AND POSTECLAMPTIC HYPERTENSION

## A Follow up Study with an Analysis of Factors Affecting the Remote Prognosis

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**I**N the present paper we shall present an analysis of a large series of postclamptic women. Of the 167 patients who were treated in 169 eclamptic pregnancies in the whole experience of the Margaret Hague Maternity Hospital 165 or 98.8 per cent, are either dead or have been re-examined recently. In addition 20 women living had eclampsia elsewhere have been examined. We shall describe the incidence of hypertension and proteinuria, the results of re-function tests, the everground findings, and general cardiovascular status at follow-up. In analysis will be shown of the several factors in pregnancy conceivably affecting the remote prognosis. Fetal mortality has been examined for the elements which seem to be of relative importance.

As early as 1851 Frenchs stated that eclampsia not infrequently is due to chronic nephritis. Many writers especially in Germany have supported this opinion, while others have discounted. Reviews of earlier publications and refers to the literature have been given by Knick (1894) Schultz (1932) Bell (1932) Lentopf and Major (1936) and Browne and (1939). In summarizing the earlier positions, Bell concluded that a mild degeneration in the renal blood vessels may often present after eclampsia.

Whether the renal lesions be hypertension found after eclampsia be attributed to the toxemia is not entirely clear for at least two reasons (1) In some cases vascular disease and hypertension antedated the eclampsia, as Teel and have recently emphasized (2) In many the follow-up studies, postclamptic path have been re-examined 15 to 30 years after eclampsia. As Volhard has said of hypertension, "the

only etiological factor about which there can be no doubt is age." Without accurate determination of the incidence of hypertension in postclamptics within periods too short for other factors significantly to affect the incidence and without a suitable control series—almost never provided—it is hard to say that a hypertension found so many years after eclampsia has been caused by the toxemia.

Estimates of the frequency of permanent hypertension after eclampsia range from 0 to 78 per cent with all intermediates, and with very few authors agreeing upon even the approximate incidence. Table I summarizes much of the published literature. A study of this table reveals that most investigations have been made by re-examining only a small proportion of the eclamptics originally observed.

Possible reasons for the wide discrepancies may be classified as (1) Often a fair sampling of the postclamptic population has not been made. (2) The majority of studies have been made with fewer than 50 patients. (3) The length of follow-up varies greatly. Furthermore the incidence of hypertension increases with age in women as well as in men, and also the question of slow healing of the vascular lesions with the eventual disappearance of hypertension has a bearing upon the problem of the frequency of sequelae.

Hevnermann and others have shown that after eclampsia many patients with residual hypertension gradually improve. On the other hand, Peckham re-examined post eclamptics at 13 months and again at about 6 years after delivery and found that the incidence of "chronic nephritis" had increased from 23 per cent to 37.7 per cent. It would seem, therefore, that variations in the time intervals of follow-up observations will affect the incidence found for hypertension.

TABLE I—SUMMARY OF THE LITERATURE DEALING WITH THE SIGNIFICANCE OF ECLAMPSIA  
—Continued

Author	Year	Clinic	Period	Cases of eclampsia	Survivors	Prenatal death	Per- cent examined	Length of fol- low up	Incidence of			Pre- natal death	Incidence of tetania
									Hypertension	Proteinuria	Chronic nephritis		
									Percent	Percent	Percent		Percent
Billings and Mordre	1936	Ohio	?	?								45	50
Blummann	1931	Duesseldorf	1911- 1915	120	?		62	1-14 yrs	6.4	1.0		35	61.9
Tula	1936	Ejota	1923- 1925	?	?	1	1	2 mos 11 yr	16.7	5.0			
Mergner	1936	Leipzig	1911- 1935	?	?	?						1.6	50
Serlentop and Major	1936	Leipzig	1921- 1932	?	?	?	16	28 mos 10 yrs	50.0	31.2			2.4
Heinzel	1937	Cottbus	?	?	?	?	30	1-37 yrs	0.0	15.4		5	0.0
Belkmann	1931	Berlin	1919- 1934	?	120	?	10	11-37 mos	0.0				
Teel and Frel	1937	Boston	1915- 1935	168	122	8	50	1-21 yr	45.0	9.0		45	31.0
Peters	1931	New Haven	1921- 1935	68	52	3	14	Up to 1 yr	25.0		43.0	15	64.5
Lane and Cox	1933	Los Angeles	1927- 1931	263	231	?	9	?	1.9			57	52.5
Titter	1935	Chicago	1921- 1935	?	103	?	45	?	11.6	15.5		3	10
Brown and Dobbs	1932	London	1911- 1935	45	45	0	40	6 mos 10 yr	10.5		0.0	5	50
Blummann and Peters	1932	Chicago	1912- 1935	51	?	?						5	52.0

fetuses of less than 1000 grams be subtracted the mortality would be 25.6 per cent.

Since there were 8 sets of twins, we have 177 babies to account for. Of these, 118 were discharged alive, 17 were stillborn, and 12 were neonatal deaths. The frequency distribution of the fetal weights and duration of pregnancy with an analysis of the survival in each group is summarized in Table II. As the pregnancy progresses and the fetus becomes larger, the rate of survival increases rapidly. Much of the adverse effect of eclampsia upon the baby, would seem to lie in the premature delivery. Yet most of the deaths are not neonatal deaths in which prematurity might be expected to be operative. The great majority 79.6 per cent of the babies lost are stillborn. Hence it seems that the older the fetus the more resistant it is to whatever intra uterine factor is so often lethal.

Extra uterine existence costs fewer infant lives than does continued intra uterine exist-

ence. This is true of all age groups and for all weight groups except those below 2000 grams. Of 144 babies born after thirty-fifth week, 28 or 19.4 per cent, were stillborn. Of the 116 born alive, 4, or 3.45 per cent died. Assuming the death rate to remain constant, delivery at thirty-fifth week would have saved 23 infant lives—could the eclampsia have been foreseen.

In carrying a toxic patient to secure an older and heavier baby, with consequent lower neonatal mortality, we postulate that the babies be born alive. It is important, therefore, to learn what will be the effect of continuing maternal toxemia upon the baby still *in utero*. A dramatic answer to this question is given in Table III. When delivery is delayed more than 3 days after the first convulsion, 57.2 per cent of the fetuses die *in utero*. Delivery within 3 days shows a stillbirth rate of 25.5 per cent—less than half that seen in cases delivered later. In postpartum eclampsia only 2.2 per cent are stillborn.



## FOLLOW UP FINDINGS

**Hypertension** Table IV summarizes our material and sets forth the incidence of hypertension found in the recent re-examinations. Counting the 5 relevant remote deaths, the incidence of outright hypertension—blood pressure above 140/90—is 17.52 per cent. If we include as hypertensives those patients with elevated systolic pressure only and those with increased diastolic pressure only then the incidence becomes 27.28 per cent. The average incidence of hypertension for 1,454 post eclampsics as summarized from 41 publications (Table I) is 19.88 per cent—chronic nephritis counted as hypertension.

The average blood pressure, at follow-up in our patients is 124/81 millimeters of mercury (Table V)

TABLE V—AVERAGE BLOOD PRESSURE

	Mean	Probable error	Standard deviation	Coefficient of variability
Systolic	124.64		19.74	64
Diastolic	80.9	78	1.70	20.1

The average age at follow up is 29.75 years, for those with hypertension the average age is 34.30 years, and for those with normal blood pressure it is 28.50 years. For the patients who showed systolic elevations only or diastolic elevation only the average age is 27.89 years. Perhaps some of these patients, when older will be outright hypertensives, perhaps in others the residual lesions will heal, and they will be normal. For convenience, these will henceforth be called 'half hypertensive'.

The average length of follow-up was 48 months for the patients having hypertension, and 52 months for those with normal blood pressure, the range for both groups is from 5 to 103 months (Margaret Hague Hospital series). In the series of women who had had eclampsia elsewhere, the average follow-up was 13 years and ranges from 4 to 27 years.

The proportion of patients with increased blood pressure is slightly lower among those who had eclampsia before 1935 though the follow-up is, of course longer. This difference is not statistically significant, for analysis by

the chi<sup>2</sup> method reveals that there are 48.6 chances in 100 for the difference to arise by a sampling error alone. Since the incidence of hypertension in these two groups is similar it might appear that post eclamptic hyperpiesia is manifested soon after the toxemia. It would then follow that re-examinations made many years after eclampsia are not especially advantageous in assessing the remote effects of the toxemia. In fact the interpretation of such long term follow-ups is complicated by the increasing incidence of hypertension in any group of older individuals. This factor of age may account for the higher incidence of hypertension which we have found in the 20 women who had had eclampsia in other hospitals. In this group the average age at follow-up is 35.4 years the incidence of hypertension is 50 per cent.

We have used 3 control series of women from the literature. Wetherby has made a study of the blood pressure distribution in 3,258 women visiting the out patient clinic in Minneapolis only cases of definite glomerulonephritis and aortic insufficiency were excluded. Blood pressures were taken with the patient sitting after having waited for some time in the clinic. Of this series, 1,544 women were in the age groups represented by our patients at follow up. The second control group is that of Alvarez and Zimmermann for 216 unmarried women drawn from the office practice of Alvarez, in California. Blood pressures were taken with the subjects recumbent, after some rest, and either the lowest or the modal pressure of several readings was accepted.

The third control series is that of Saller who analyzed the blood pressures of 1,743 women attending the out patient clinic at Kiel 99 per cent of these subjects were of the laboring class. Patients excluded from the analysis were those with recognizable renal disease, anemia, hormonal disturbances, and diabetes. Blood pressures were taken after the patients had waited at least half an hour in the clinic. Of Saller's series, 1,142 women were in the same age groups as our post eclamptics.

The age groups of these various control series were weighted so as to correspond with the age distribution in the post eclamptic

women, and the data of the three series were combined. The corrected frequency curves were then drawn in Figure 1, which also compares the blood pressures found in our post-eclampsics. The 3 curves drawn from the published data of the authors cited are strikingly similar, for the systolic pressure and are very nearly parallel over the whole range of blood pressures observed. The diastolic curves are not in such good accord. These data, then, give a fair index of the frequency of increased blood pressure in a large group of women (2,902) who are living under diverse conditions.

As one compares the control curves with that for the post-eclamptic women, it is apparent that there is a slightly increased incidence of hypertension among the patients who have had eclampsia. Of all the control series, Wetherby's shows the highest proportion of women with elevated blood pressures. Accordingly, this series has been taken for comparison in analyzing the statistical significance of the findings in the post-eclampsics (Table VI).

TABLE VI—CONTROL SERIES, CORRECTED FOR AGE

	Systolic greater than		Diastolic greater than	
	140 mm Hg	150 mm Hg	90 mm Hg	100 mm Hg
	Per cent	Per cent	Per cent	Per cent
Wetherby	14.84	8.25	20.7	5.1
Alvarez and Zimmermann	16.76	5.56	6.51	1.1
Saller	6.89	2.67	23.4	13.1
Posteclampsics	18.0	13.1		

It is only at pressures above 150 systolic and 100 diastolic that the post-eclampsics show significantly higher incidences than do Wetherby's women.<sup>1</sup>

We may conclude, then, that there is an increased incidence of hypertension among

<sup>1</sup> Dividing each of the series at these pressures, constructing four fold tables and solving for  $\chi^2$  in order to get the probabilities, we find that there really is a significant difference in the control and post-eclamptic groups. There are only 4 chances in 100 that the difference between Wetherby's corrected curve and the curve for the post-eclampsics could arise by sampling error—considering the portion beyond 150 millimeters of mercury for the systolic pressure. For the curves beyond diastolic pressures of 100 millimeters of mercury, there are but 63 chances in 100,000 that sampling errors could give the difference.

post-eclamptic patients, this difference is statistically significant.

**Proteinuria** In 123 of the 159 patients, or 77.2 per cent, no protein was detected in 32, or 20.2 per cent. As mentioned, the sulfosalicylic acid method was used. By the boiling and acetic acid test, the great majority of these urines would have been negative. Moreover, voided specimens were taken for the analysis. Short and Ley have recently demonstrated as much or more urinary protein in 20 to 31 per cent of nearly 5,000 women. We believe life insurance policy holders therefore, that no significance can be attached to the minimal amounts of urinary protein in these 32 post-eclamptic subjects.

One patient, with a normal blood pressure at 97 months after eclampsia and her last delivery, showed a trace of protein in a voided specimen. Another, A. E., whose case is described under the remote deaths, had a 2 plus (about 3 grams per liter) proteinuria. The third patient to have a proteinuria of significant degree is described under the remote deaths (R. T.). She ran 8 to 10 grams per liter of protein until going into terminal uremia, she was the only patient to show urinary casts in significant numbers. In this case, renal disease was known to have antedated the eclamptic pregnancy.

In summary, only 3 patients had proteinuria of possibly significant degree. One of these was a chronic nephritic before her pregnancy, and one was probably a chronic hypertensive before eclampsia.

**Urea clearance** Urea clearances were done in 131 cases at follow-up. An additional 21 patients attained urinary specific gravities higher than 1.025 in casual urines, since protein and sugar were absent, urea clearances were not done because they would have been normal.

In only 5 cases was the clearance found to be less than 60 per cent, and therefore sub-normal. In 2 of these, hypertension without proteinuria was also found. One patient was the remote nephritic death (R. T.). In the 2 others, the lowered urea clearance was the only positive finding, and perhaps repetition of the test would give normal readings. In

any normal subject the urea clearance does occasionally fall below 60 per cent in the wide variations which may be observed.

The average clearance is somewhat lowered, both in patients with normal blood pressure and in the hypertensives (Table VII). Possibly the average would have been closer to the ideal 100 per cent if clearances had been done on the patients with high urinary specific gravities, for with their omission there is a factor of selection.

TABLE VII.—UREA CLEARANCE

	Cases	Mean, as per cent of average normal	Standard deviation
Patients with normal blood pressure	97	86	16.66
Hypertensives	26	84	6.9

**Blood chemistry.** For want of space we shall merely say that the blood levels of non-protein nitrogen, urea nitrogen, and uric acid were always found to be within normal limits except in the case of the remote nephritic death (R. T.)

The blood sugar was pathologically increased in 3 cases. In 2 of these blood sugars were normal at the time of the eclampsia and in the puerperium. Diabetes had become manifest in the interim.

**Physical examination.** Of the 38 hypertensive patients seen at follow up, 19 had cardiac enlargement either by physical signs or by x-ray examination. Of these, 2 cases were associated with rheumatic heart disease. Eight of the patients had signs and symptoms of cardiac insufficiency. One was admitted to the hospital during the course of the follow up in cardiac failure with the diagnosis of hypertensive cardiovascular disease.

Special interest was attached to the eye ground findings since their importance has been emphasized by Corwin and Herrick and by others as substantiating the nature of the hypertension following toxemia. Of the 38 hypertensive patients, 26 had satisfactory eye ground examinations. Four had died with no record of fundus readings, 3 were not examined because they were seen in the home and in 2 the pupils were too contracted for satisfactory examination. Since the patients were unac-

companied to the clinic, in many cases, dilatation of the pupils was omitted.

Of the 26 examined, 23 had definite eye ground changes. In 19 this consisted of attenuation of the arterioles with or without irregularity of the lumen. In 4 irregularity of the arteriolar lumen was noted, although the arterioles in general were of average caliber as compared with the veins. In 9 patients compression of the vein at the arteriolar crossing was noted. The light reflex was so increased in 9 patients as to excite a special note. In 2 the wall of the attenuated artery looked unusually heavy with the lumen reduced to a thready line. In 1 patient hospitalized in cardiac failure edema of the discs appeared and in another "albuminuric retinitis" with exudate and hemorrhage was seen. Marked choroidal change was present in 2 instances.

The findings in the half-hypertensive group of 11 patients confirmed our impression that these included a high percentage of cases which would become outright hypertensive cases on later examination. Of the 8 patients investigated for fundus changes, 4 showed abnormalities: 2 had irregularity of the arteriolar lumen and 2 general attenuation of the arterioles.

Among the patients with normal blood pressure there were 4 instances of significant eyeground changes. Two had thickening of the arteriolar walls, increased light reflex but no irregularity in caliber. Two showed irregularity of the arterioles without change in the general caliber of the vessels.

The radial arteries were palpated in each case, but it was not felt that any information about the state of the vascular system was obtainable in this way, which could not be more reliably ascertained by other means.

In 7 patients still surviving the full blown picture of high blood pressure, radial artery sclerosis, eyeground changes, and cardiac enlargement was present.

#### FACTORS AFFECTING THE PERSISTENCE OF HYPERTENSION

In analyzing the elements which seem to contribute to the persistence of hypertension, we find that some are amenable to control,



strated the incidence of post eclamptic hypertension increases with the parity of the patients.

TABLE XII—PARITY

Parity	I	II	III	IV and more
No. cases	60		30	34
Per cent hypertensive			30	47
Per cent half hypertensive	8	8		
Per cent normal	7	78	17	47

Since in general the patients of higher parity are older we have tried to separate the factors of age and number of births, though there are not enough cases to give clear-cut results in all age groups. The analysis, shown in Table XIII, indicates that parity, independently of age, seems to be a governing factor in the persistence of hypertension. However this may in turn be explained by the occurrence of other toxemias in some of the pregnancies.

*Time of onset and duration of toxemia.* As has been pointed out in the introduction, two factors—time of onset and duration of toxemia—have not been hitherto separated in analyzing their influence upon the finding of hypertension at follow-up examination. It is especially important to make this differentia-

TABLE XIII—RELATION OF PARITY INDEPENDENTLY OF AGE, TO SUBSEQUENT HYPERTENSION AFTER ECLAMPSIA

Status at follow-up		No.	Hypertensive	Half hypertensive	Normal
Age	Parity	No.	Per cent	Per cent	Per cent
21	I			8	8
	II		10	16	16
	III	10		30	30
	IV +	17		35	35
25-30	I	17		35	35
	II	17		35	35
	III		35		35
	IV +	8	37		60
30	I		16	8	72
	II		20		80
	III		30		30
	IV +				37
41+	I, II, III		42.8	26.8	28
	IV and more		50	30	20

tion because it has a self-evident bearing upon the treatment of antepartum eclampsia.

In 1878 Schroeder suggested that the longer a patient was carried with toxemia, the more likely she was to have a chronic nephritis later. Perhaps the first to publish quantitative studies on the question was Gibberd. He found that in 38 previously normal women, in whom pregnancy was terminated within 3 weeks after the appearance of toxemia, only 5 per cent developed "chronic nephritis." Among 29 previously healthy patients in whom the toxemia was allowed to continue for more than 3 weeks 38 per cent developed signs of "chronic nephritis." The recurrence rates of toxemia in subsequent pregnancies were 36 and 76 per cent, respectively. Disregarding the fact—as Gibberd did—that patients carried for longer periods must often have earlier onsets of toxemia, it seems logical to consider that exposure of the vascular system, including the blood vessels of the kidney to continuing toxemia may cause progressive damage. The hypertension found at follow-up then might be said to be caused by the toxemia.

When toxemia onset is considered without regard to its duration, early appearance seems to be associated with an increased incidence of hypertension at follow-up. Disregarding the duration of toxemia the gross incidences of

TABLE XIV—ELEVATED BLOOD PRESSURE AT RE EXAMINATION

Toxemia onset	Follow-up findings		
	Hypertensive Per cent	Half-hypertensive Per cent	Normal Per cent
Before seventh month	44		57
Seventh to eighth month	20	20	60
Eighth to ninth month	10	1	77.8

TABLE XV—DURATION OF TOXEMIA

Duration of toxemia	Follow-up findings		
	Hypertensive Per cent	Half-hypertensive Per cent	Normal Per cent
Less than 3 weeks			77
More than 3 weeks	47.7		47.7

TABLE XVI—RELATION OF DURATION OF TOXEMIA TO SUBSEQUENT HYPERTENSION

Findings at follow up	Onset of toxemia					
	Before 7th month		7th-8th month		8th-9th month	
	Carried with toxemia					
	Less than 3 weeks	More than 3 weeks	Less than 3 weeks	More than 3 weeks	Less than 3 weeks	More than 3 weeks
	Per cent	Per cent	Per cent	Per cent	Per cent	Per cent
Hypertension	14.3	63.6	0.0	60.0	10.3	12.5
Half hypertension	14.3	0.0	20.0	20.0	12.0	25.0
Normal	71.4	36.4	80.0	20.0	77.7	62.5

elevated blood pressure at the re-examination are shown in Table XIV. Similarly when the duration is considered alone, an increased incidence of hypertension parallels longer duration (Table XV).

However, when we examine in each case the effect of onset in terms of the duration of the toxemia, as in Table XVI, it is seen that the important factor of the two is duration of the toxemia, the time of onset, *per se*, does not significantly affect the remote prognosis. When the toxemia appeared in the seventh month, a high proportion of patients were carried for several weeks before delivery, in the interests of the fetus. This longer average duration of toxemia masks the fact that a patient having toxemia appearing in the seventh month—if promptly delivered—is no more likely to have permanent hypertension than is the woman who has toxemia appearing at term.

*Severity of toxemia.* Our data accord with what several previous writers have pointed out, a definite correlation can be drawn between the severity of the eclampsia and the incidence of subsequent hypertension. When the systolic blood pressure, in eclampsia, averages less than 180 milligrams of mercury, 10.66 per cent of the patients had hypertension at follow-up. The level of blood pressure and degree of proteinuria, below this point, do not seem to influence the appearance of persistent hypertension. In those cases in which the systolic blood pressure, during eclampsia,

averages more than 180, the incidence of persistent hypertension jumped to 44.8 per cent (Table XVII).

TABLE XVII

	Blood pressure less than 150		Blood pressure 151-180		Blood pressure 181-200		Blood pressure more than 200	
	Proteinuria	Proteinuria	Proteinuria	Proteinuria	Proteinuria	Proteinuria	Proteinuria	Proteinuria
	<2+	>2+	<2+	>2+	<2+	>2+	<2+	>2+
No cases	23	24	17	58	2	19	1	7
Per cent hypertensive	13.05	16.67	5.89	8.62	0	47.4	100	42.9
Per cent half hypertensive	4.35	8.33	5.89	12.07	0	15.8	0	28.6
Per cent normal	82.60	75.00	88.22	79.31	100	36.8	0	28.6

*Blood pressure and proteinuria at 10 days and 6 weeks postpartum.* Future hypertension cannot be predicted with any confidence from the blood pressure and urinary protein findings at 10 days or at 6 weeks after delivery. However, patients who have not returned to normal within this period are considerably more liable to subsequent hypertension (Table XVIII).

TABLE XVIII

	No cases	Hypertension in follow up Per cent
Blood pressure normal at 10 days	99	13.13
Blood pressure high at 10 days	58	37.92
Blood pressure high at 6 weeks	15	46.70
Proteinuria less than 2 grams per liter at 10 days	107	11.22
Proteinuria more than 2 grams per liter at 10 days	41	46.30

*Weight/height ratio at follow-up.* Hypertension generally is more common in individuals who have high weight/height ratios, i.e. in the obese. The incidence of hypertension in our post eclamptics shows this same relation to obesity (Table XIX).

TABLE XIX—WEIGHT/HEIGHT RATIO

Weight/height ratio	No cases	Hypertension Per cent	Half hypertension Per cent	Normal Per cent
Less than 1.80	22	4.5	0	95.5
1.81-2.60	77	13.0	7.8	79.2
More than 2.61	23	30.4	26.1	43.5

TABLE XX—RELATION OF SUBSEQUENT PREGNANCIES TO THE INCIDENCE OF POST ECLAMPTIC HYPERTENSION

Subsequent pregnancies	Case	Status at follow up					
		Hypertensive		Half hypertensive		Normal	
		Cases	Per cent	Cases	Per cent	Cases	Per cent
None	37		30.5	7	6	65	73.8
One	49		24.5	3	30	36	
Normal			6		6	27	67.4
Total	77	8	39		13		81.8
			25				34.2
Two			6		16		3
Both normal							
One normal One toxic	6	3	30				50
Both toxic	3		60				60
Three			40			6	60
Four	4	1	25				1

Since weight reduction in overweight patients will often reduce the blood pressure (Ley) it would therefore seem that the control of obesity might be of value in post eclamptic patients.

**Subsequent pregnancies** One of the most practical questions arising for the remote prognosis in a patient who has had eclampsia is that of further pregnancies. We have seen many post eclamptic patients in whom no abnormality can be found and who have been warned against any further pregnancy. In a few cases therapeutic abortions have been done (elsewhere) because of the eclamptic history alone. Many publications lend support to these steps.

We have made an analysis of the 84 post eclamptic patients who have had subsequent pregnancies, and compared them with the 93 patients who have had no later pregnancy.

From the data in Table XX, it appears that one or two subsequent normal pregnancies will not affect adversely the remote prognosis. A subsequent toxic pregnancy, however, will increase markedly the chances for a persistent hypertension.

It is interesting to note that if one subsequent pregnancy occurs, and if it is toxic, the incidence of hypertension at follow-up is

about 50 per cent. When 2 subsequent pregnancies occur 1 normal and 1 toxic, the normal pregnancy does not seem to count, and the toxic pregnancy exerts its same effect—the incidence of hypertension is again found to be about 50 per cent.

We have made an analysis of the effect of all pregnancies, before and after eclampsia. Since the incidence of hypertension is lowest among patients who have had only the one (eclamptic) pregnancy and almost equally low among those whose other pregnancies have been normal, it seems that perhaps the most important single factor in determining future hypertension is another toxemia (Table XXI).

TABLE XXI

Follow up ending	No other pregnancy	Other pregnancy normal	Other toxemia later	Other toxemia	
				Known toxemia	Unknown
No cases	23	45		47	3
Per cent hypertension	6.5	8.9	30.8	41	6
Per cent late hypertension	8.6				
Per cent normal	81.4	91.1	69.2	42.5	37.5

The incidence of hypertension is so low in post eclamptic patients who have had no other toxemia, that we may question whether eclampsia alone does cause remote hypertension. Taking the data at face value it might seem that eclampsia merely predisposes the patient to toxemia which in turn causes the hypertension found at follow up. Of the 38 post eclamptic hypertensive patients, 26 or 68.4 per cent, are known to have had at least one other toxic pregnancy, 8, or 21 per cent, are known not to have had another toxemia and in 4 cases this is uncertain.

#### RECURRENT OF TOXEMIA

Of all the post eclamptics, 90 patients have had 143 subsequent pregnancies, 26 or 18.17 per cent of these terminated in abortions, 16 or 11.18 per cent, in stillbirths and 101 or 70.65 per cent, in live births. Thus the fetal losses in later pregnancies almost exactly match those present in the eclamptic pregnancy group.

Thirty-seven of the 84 patients carrying their pregnancies past the twenty-fourth week had 55 toxemias, or 47 per cent, of which 2, or 2.38 per cent, were again eclamptic. The published data from Table I show 881 women pregnant after eclampsia, with a toxemia recurrence of 39.3 per cent. However, many of these papers do not include mild toxemias, but only count recurrent eclampsia and severe toxemia.

Prenatal care did not seem to avail much in reducing the rate of recurrence in toxemia, though the incidence of severe toxemia is probably diminished by such care (Table XXII).

TABLE XXII—PRENATAL CARE

	No care	Private care	Clinic care	
			Less than 2 mo	More than 2 mo
Pregnancies	11	31	28	46
Toxic, per cent	54.5	48.4	53.5	41.3

The age of the patient at the time of eclampsia is directly related to the recurrence of toxemia in subsequent pregnancies (Table XXIII).

TABLE XXIII—AGE WHEN ECLAMPTIC

	15-20	21-25	26-30	31-35	36-40
Recurrence of toxemia per cent	37.15	41.95	55.60	71.50	100

The severity of the eclampsia affects the recurrence rate of toxemia in later pregnancies (Table XXIV).

TABLE XXIV

	Average blood pressure in eclampsia			
	Less than 150 mm	151-180	181-200	More than 201
Pregnant again	29	7	8	2
Toxic in later pregnancy per cent	20.7	48.1	62.5	100

We cannot assess the influence of time of onset and duration of toxemia independently, because we have too few cases in which the necessary data are known. However, in 66 cases (51 patients) we do know the duration

of toxemia in the eclamptic pregnancy. As shown in the analysis, any patient carried with toxemia for more than 2 weeks is more likely to suffer later toxemia (Table XXV).

TABLE XXV

Duration of toxemia in eclamptic pregnancy	Subsequent pregnancies	Toxemias per cent
Less than 2 weeks	39	70.5
More than 2 weeks	27	63.0

Subsequent pregnancy, to restate an idea current in the literature, is a delicate test of the damage left by a toxemia. While the severity of the eclampsia does affect the remote incidence of persistent hypertension, the effect is more clearly seen in the recurrence rate of toxemia. Similarly, duration of toxemia affects the later appearance of hypertension, but toxemia of even shorter duration has an equally marked effect upon the recurrence of toxemia.

It is a common practice to warn post-eclamptic patients against having another pregnancy "too soon." This serves to cut down the total number of pregnancies, which is beneficial as we have seen above. This recommendation also carries the implication

TABLE XXVI

	Interval from eclampsia to conception					
	Less than 3 months	3-6 months	7-12 months	13-24 months	25-36 months	More than 37 months
No pregnant again	4	7	14	18	16	14
Per cent toxic in first pregnancy after eclampsia	50	71.5	64.2	55.7	31.2	50.0

that after eclampsia the damage inflicted may heal gradually. On the basis of the few cases available we have sought for a relationship between the interval from eclampsia to conception and the recurrence of toxemia. There seems to be a rough trend to indicate that the longer the interval, the less the chance of having a recurrent toxemia (Table XXVI).

## SUMMARY AND CONCLUSIONS

The immediate maternal mortality, in a series of 169 cases of eclampsia, was 7.10 per cent, uncorrected.



The fetal losses, including all cases were 33.5 per cent. The chief source of fetal loss is stillbirth. The factors contributing to the death rate are prematurity and duration and severity of the maternal toxemia.

An analysis is presented of the eclamptic pregnancies as a basis for an assessment of the effects of various factors in pregnancy upon the persistence of hypertension.

Of the 155 women surviving eclampsia, 8 have died subsequently. 5 deaths were in the field of cardiovascular and renal disease.

The incidence of hypertension at follow up in the Margaret Hague Maternity Hospital series, was 17.5 per cent in the women who had had eclampsia elsewhere it was 50 per cent. An additional 9.8 per cent of the former had a systolic or a diastolic elevation alone.

The incidence of hypertension among the post-eclamptic patients is significantly greater than in the female population at large, correction being made for age distributions.

The incidence of proteinuria of significant degree is 2.6 per cent at follow up.

Renal function as measured by the urea clearance and urinary specific gravity is in the normal range in at least 97 per cent of the patients at follow-up.

The majority of the living hypertensives had significant eyeground findings. Half had cardiac enlargement and 8 had signs and symptoms of cardiac insufficiency.

An extensive analysis has been made of the factors contributing to the persistence of hypertension. In general we may say that high blood pressure is more likely to be found at follow up if there is antecedent renal or vascular disease. Also the higher the first observed blood pressure in pregnancy—even in the normal range—or the older the patient when eclamptic or at follow-up or the more children she has had or the longer she is carried with toxemia, or the more severe the eclampsia, or the more obese the patient, the more likely hyperplasia is to persist. The time of onset of toxemia, whether in the seventh month or at term, has no direct effect upon the remote prognosis. Early onset often seems to favor future hypertension only because the patients are carried for considerable periods before delivery.

None of the above considerations is so decisive in conditioning remote hypertension as is recurring toxemia subsequent to the eclampsia. Hypertension is not often found in a woman who has had a single eclampsia as the only toxemia of pregnancy. Most of the post-eclamptic hypertensives have had an other toxemic pregnancy.

The recurrence rate of toxemia in pregnancies after eclampsia was found to be 47 per cent. In general, the factors enumerated above which favor the persistence of hypertension favor in even greater degree the recurrence of toxemia.

After the thirty-fifth week of gestation, the fetus fares much better *ex utero* in eclampsia.

In subsequent pregnancies after eclampsia the fetal losses were 29.4 per cent.

Advising against future pregnancies in a post-eclamptic would seem to be justified by the recurrence of toxemia in 47 per cent of cases, with a consequent 8 fold increase in chances for permanent hypertension if the pregnancy is toxic.

In evaluating a given patient's risks in a future pregnancy one may consider the present blood pressure, the severity of the past eclampsia, duration of that toxemia, obesity, age, and interval since the eclamptic pregnancy.

We wish to express our grateful appreciation to Dr. S. A. Congro, for his painstaking criticism of this paper. Drs. J. F. Norton and E. G. Walters have also made helpful suggestions. We are indebted to many physicians who have permitted us to re-examine their private patients, and to the many people who have co-operated in finding lost patients. Many of the blood and urine were examinations were done by Francis Omlat and Peter Marotta. Mrs. E. R. Chesley assisted in finding and examining patients.

#### BIBLIOGRAPHY

1. ABEL, W. C. and ZUCKERMAN, A. Blood pressure in women as influenced by the sexual organs. *Arch. Int. Med.*, 1916, 37, 597.
2. BIRCH, Untersuchungen über das spätere Schicksal bei und mercurieller Schwangerer. *Verhandl. d. deutsch. Gynäcol. Kongresses*, 1914, 5, 40.
3. BELL, E. T. Renal lesions in the toxemias of pregnancy. *Am. J. Path.*, 1934, 4.
4. BOKELMANN, O. Das Endprognose der Nephropathia und Eklampsia gravidarum in ihrer Beziehung zur Krankheitsdauer. *Ztschr. f. Geburtsh. u. Gynäcol.*, 1937, 5, 937.
5. BRIDGES, J. An inquiry into the after effects of eclampsia with special reference to hypertension and chronic nephritis. *Lancet*, 1934, 43.

- 6 BROWNE, F J, and DODDS, G H The remote prognosis of the toxæmias of pregnancy, based on a follow up study of 400 patients in 589 pregnancies for periods varying from 6 months to 12 years *J Obst & Gynec Brit Emp*, 1939, 46 443
- 7 BUND, R Ueber das späetere Befinden Eklamptischer und ihrer Kinder *Zentralbl f Gynaek*, 1925, 49 2879
- 8 CALDWELL, W, and LYLE, W The blood chemistry in normal and abnormal pregnancy *Am. J Obst & Gynec*, 1921, 2 17
- 9 CLOW, F E After effects of toxemia of pregnancy *New England J Med*, 1928, 198 351
- 10 COLAVECCHIO, A, and PRISTER, B Esiti lontani delle eclamptische, preeclamptische e dei loro figli *Ann di ostet e ginec*, 1932, 54 1865
- 11 CORWIN, J, and HERRICK, W W Toxemias of pregnancy in relation to chronic cardiovascular and renal disease *Am J Obst & Gynec*, 1927, 14 783
- 12 DIECKMANN, W J, and BROWN, I Do eclampsia and pre-eclampsia cause permanent vascular renal pathology? *Am J Obst & Gynec*, 1939, 37 762
- 13 DOEDERLEIN, G Nachuntersuchungen an ehemals Eklamptischen *Arch f Gynaek*, 1925, 125 655
- 14 EFFKEMANN, G Ueber spaetschaeden der Niere nach ueberstandener Toxikose und der Einfluss spaeterer Schwangerschaften auf die Restzustaende renaler Gestose *Arch f Gynaek*, 1935, 159 493
- 15 Idem Ueber den Einfluss spaeterer Schwangerschaften nach ueberstandenen Toxikose auf die Nierenfunktion *Zentralbl f Gynaek*, 1936, 60 453
- 16 FRIEDRICHS Quoted by Koblanck
- 17 GIBBERD, G I The significance of recurrence in the late toxæmias of pregnancy *J Obst & Gynec Brit. Emp*, 1934, 41 23
- 18 GIBSON, H K The sequelae and later aspect of the toxic albuminurias of pregnancy *Surg, Gynec & Obst*, 1921, 32 513
- 19 GREENHILL, J P Eclampsia at the Chicago Lying-In Hospital *J Am M Ass*, 1926, 87 228
- 20 GREIFENSTEIN, J Ueber Eklampsie und das späetere Schicksal ehemals eklamptischer Frauen *Inaugural Dissertations*, Bonn, 1931
- 21 HARRIS, J W The after-effects of the late toxemias of pregnancy *Bull Johns Hopkins Hosp*, 1924, 35 103
- 22 HEINEVEITER, A Ueber spaetschaeden nach Eklampsie *Inaugural Dissertations*, Goettingen, 1937
- 23 HERRICK, W W, and TILLMAN, A J B Toxemia of pregnancy Its relation to cardiovascular and renal disease, clinical and necropsy observations with a long follow up *Arch Int Med*, 1935, 55 643
- 24 HEYNEMANN, T Spaetfolgen der Eklampsie und ihrer Vorstadien unter besonderer Beruecksichtigung der Nierenveraenderung *Zentralbl f Gynaek*, 1934, 58 3010
- 25 HINSELMANN, H. Die Eklampsie *Bonn Friedrich Cohen*, 1924
- 26 HUBING, W Die Eklampsien und das späetere Schicksal eklamptischer Frauen *Inaugural Dissertations*, Frankfurt, 1932
- 27 JENSEN, J The Heart in Pregnancy *St Louis C V Mosby Co*, 1938, pp 319-322
- 28 KJELLAND MØRDRE, S Våre eklamptipatienters skæbne under senere svangerskap og fødsler *Norsk Mag f Laegevidensk*, 1935, 96 712
- 29 KOBES, R Das späetere Schicksal eklamptischer und preeclamptischer Frauen *Zentralbl f Gynaek*, 1930, 54 666
- 30 KOBLANCK Zur Prognose der Schwangerschaftsnephritis *Ztschr f Geburtsh u Gynaek*, 1894, 29 268
- 31 LE PAGE, G Prognostic éloigné de l'albuminurie chez les femmes encientes *Ann de gynéc et d'obst*, 1912, 9 577
- 32 LEY, H A The effect of change in weight on blood pressures as shown in a study of 3,516 examinees *Proc. Life Extension Examiners*, 1939, 1 33
- 33 MERGNER, E Eine Untersuchung ueber den Verlauf späetere Schwangerschaften nach Eklampsie *Inaugural Dissertations*, Leipzig, 1936
- 34 MUSSEY, R D Recurring pre eclamptic toxemia its clinical significance *Minnesota Med*, 1931, 14 889
- 35 NEUWIRTH Nachuntersuchungen an ehemals Eklamptischen *Inaugural Dissertations*, Wuerzburg, 1926 (Quoted by Hubing)
- 36 NEVERMANN, H Ueber das weitere Schicksal der an Eklampsie erkrankten Frauen *Arch f Gynaek*, 1927, 129 891
- 37 NURI, M Zur Frage der Spaetschaedigungen des Gefaesssystems nach Eklampsie und Praeeklampsie *Monatschr f Geburtsh u Gynaek*, 1936, 102 282
- 38 OLSEN, A Vore eklamptipatienters senere skæbne *Ugesk. f Laeger*, 1933, 95 1019
- 39 PAGE, E W, and COX, A J Renal changes following toxemias of late pregnancy *West J Surg*, 1938, 46 463
- 40 PECKHAM, C H Chronic nephritis following eclampsia *Bull Johns Hopkins Hosp*, 1929, 45 176
- 41 Idem The incidence, differential diagnosis, and immediate and remote prognosis of the toxemias of late pregnancy *J Michigan State Med Soc*, 1936, 35 301
- 42 PETERS, J P Toxemias of pregnancy *Yale J Biol & Med*, 1937, 9 311
- 43 RUCKER, M P The late sequelae of eclampsia *Am J Obst & Gynec*, 1932, 23 211
- 44 SALLER, K Ueber die Altersveraenderungen des Blutdrucks *Ztschr f d ges exper Med*, 1928, 58 683
- 45 SCHMIECHEL, A Ueber die rezidivierende Eklampsie *Zentralbl f Gynaek*, 1929, 53 2405
- 46 SCHROEDER. Verhandlung Aertliche Gesellschaften, Sitzung vom 14 Mai 1878 *Berl klin Wchnschr*, 1878, 15 559
- 47 SCHULTZ, W Das späetere Schicksal der an Eklampsie und Schwangerschaftsnier Erkranken Muenchen med Wchnschr, 1932, 79 2038
- 48 SEIDENTOPF, H, and MAJOR, H Die Spaetfolgen der eklamptischen Schwangerschaftserkrankungen *Arch f Gynaek*, 1936, 160 601
- 49 SEITZ, L Zur Symptomatologie, Prophylaxe und Therapie der Eklampsie und ihrer Vorstufen *Arch f Gynaek*, 1930, 142 52
- 50 SHORT, J J, and LEY, H A The incidence of albuminuria with red cells and casts and of glycosuria at different age periods among 10,000 unselected examinees *Proc Life Extension Examiners*, 1939, 1 134
- 51 SYM, J C B The ultimate prognosis in cases of eclampsia and albuminuria of pregnancy *Lancet*, 1929, 2 698
- 52 TEEL, H M, and REID, D L Eclampsia and its sequelae *Am J Obst & Gynec*, 1937, 34 12
- 53 TIGGES, H A. Das späetere Befinden der Frauen, die eine Eklampsie oder Praeeklampsie ueberstanden haben *Inaugural Dissertation*, Koeln, 1938

54. THOMPSON, S. On the subsequent state of health of the patients of eclampsia. *Jap J Obst. & Gynec.* 936, 9, 475.
55. VAN SICKLE, D. D. Determination of urea by gravimetric measurement of the carbon dioxide formed by the action of urease. *J Biol. Chem.* 9, 7, 73, 695.
56. VOLLMER, F. Elevated blood pressure. I. The Kidney in Health and Disease. Philadelphia: Lea and Febiger, 935.
57. WAGNER, R. Die Symptomatologie und das seltene Schicksal der Eklampsie und der Präeklampsie. *Insurgural Dissertation, Basel.* 934.
58. WEISSER, M. A comparison of blood pressure in men and women based upon statistical study of the cases of 5540 individuals. In *The Kidney in Health and Disease*. Philadelphia: Lea and Febiger, 935.
59. WOLFF, P. and ZADY, M. Zu Diagnose und Prognose der Nierenveränderungen in der Schwangerschaft. *Monatsschr. f. Geburtsh. Gynaek.*, 94, 40, 699.
60. ZONDER, B. and JACOBOWITZ. Ueber das Schicksal von Frauen, die eine Gestationsstörung (Nierenkränkung, Eklampsie) durchgemacht haben. *Klin. Wochenschr.* 924, 3, 15.

# A STUDY OF THE CLINICAL MANIFESTATIONS AND THE RESULTS OF TREATMENT OF TWENTY-TWO PATIENTS WITH RAYNAUD'S SYMPTOMS

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THE symptom complex commonly known as Raynaud's disease has received an unusual amount of attention in medical literature since its original classical description by Raynaud in 1862 (7, 8). Little has been added to the original description or theories, however, and Lewis (6) states that, "just as Raynaud's description stands, so his views of the malady predominate today."

It was recognized early that what is known as Raynaud's disease is probably not a disease but a symptom complex, the objective manifestations of which have a multiple etiology. John Hunt, in his recent review of the subject, stated, "nearly fifty years ago Hutchinson recognized clearly the true significance of Raynaud's thesis, and in his writings he stressed the fact that, 'Raynaud's phenomenon,' as he called it, was not a clinical entity at all but a syndrome occurring in many different conditions." Hunt subscribes to this view, but believes that the term Raynaud's disease is so well established it will continue to be used whether it has any meaning or not.

One is impressed with the wide difference of opinion regarding the nature and etiology of Raynaud's symptoms, the diagnosis, and whether what is known as Raynaud's disease even exists as a clinical entity. Allen and Brown, reviewing Raynaud's 26 original cases, concluded that only 6 could be classified as having Raynaud's disease. Hunt, reviewing the same cases, concluded that only 1 of the series had Raynaud's disease, and this one was doubtful. He stated that even if Raynaud's disease exists, it must be rare.

A wide difference of opinion exists regarding the nature and cause of the vascular phenomena observed in Raynaud's attacks. Raynaud thought the spasms were due to an abnormal vasomotor tone. Lewis thinks the attacks are due to a "local fault" with normal vasomotor tone.

This confusion and difference of opinion is reflected in the modes of treatment. Persons subscribing to abnormal vasomotor tone advocate operations on the sympathetic nervous system; those thinking the spasms due to a local fault use

general measures in an attempt to avoid attacks and to correct the local fault.

Realizing the controversial nature of all aspects of the subject, it is with hesitation that I add another report which offers no solution. But this report is believed to be justified by its presentation of a new method of attack, some new ideas on the state of the vascular system, and the results of medical as contrasted with surgical management. This study involves the history, physical findings, laboratory findings, treatment, and course of 22 patients with Raynaud's symptoms in the hands, or in the hands and feet. Raynaud's symptoms never occurred in the feet alone.

To conserve space and illustrations, the detail concerned with the patients is summarized in tables. Table I is a summary of the patients' histories. Although self-explanatory, a few findings require some comment. There are two colored patients in this series: one male and one female. No reports of Raynaud's disease in the colored race could be found.

In this series, all the patients had Raynaud's symptoms in the fingers; 11 had similar symptoms in the toes, but in no case did the symptoms occur in the toes without the patient being subject to the symptoms also in the fingers. In only one of the patients with Raynaud's symptoms in the toes were the symptoms severe enough to require any particular care. A lumbar sympathectomy was done on this patient; the results are reported in detail in the case report of Mr. Y.

Emotional spells as a cause of Raynaud's symptoms are worthy of comment. In only 3 of the patients were they a frequent cause and in these 3 sympathetic surgery failed to produce any improvement as judged by recurrence of symptoms and the frequency and severity of attacks.

Table II is a summary of the laboratory findings and associated diseases. Associated diseases are comparatively common in this series: 2 had syphilis, 13, a mild secondary anemia, 2, a severe anemia, 3, stiffness of the finger joints, scleroderma, ulcers, loss of tissue, and loss of fingernails, and, 2 had sclerodactylia. It is very interesting to note that the scleroderma, stiffness of

From the Department of Medicine, Northwestern University.

TABLE I.—SUMMARY OF HISTORICAL FINDINGS

Sex	No. of cases
Females	8
Males	4
Race	
White	30
Colored	
Age (onset)	
years	
0-10 years	
10-20 years	5
20-30 years	7
30-40 years	6
40-50 years	
50-60 years	
Site of Raynaud's symptoms	
Fingers	
Fingers and toes	
Toes, not fingers	
Severity of symptoms—in hands	
Mild	
Severe	9
in feet	3
Mild	
Severe	
Noted in family history	
Symptoms	3
Local pallor	
followed by	
Local cyanosis	
followed by	7
Local rubor	
Attacks caused by	
Cool air, most easily	
Cool water, less easily	
Chilling of body by cold drink	
Emotional spells	7
occasionally	
frequently	6
Attacks relieved by	
Immersion of hands in warm water	6
Immersion of hands in cold water followed by	
arm	
Slaking of hands	
Robbing of hands	3
Warm air	3
Influence of seasons	
Worse in winter (+)	
Mildly cold (2-3+)	
Present in summer (+)	6
Presence of associated findings—in scores of	
following:	
Loss of fingernails	3
Loss of tips of fingers	5
Scleroderma	5
Sclerodactylia	3

TABLE II.—SUMMARY OF LABORATORY EXAMINATION

	Case
Red blood count	
3 to 3.5 million	
3.5 to 4 million	
4 to 4.5 million	5
4.5 to 5 million	4
5 to 5.5 million	3
Hemoglobin— <sup>g</sup>	
55 to 50	
60 to 64	
65 to 69	
70 to 74	6
75 to 79	
80 to 84	5
85 to 89	
90 to 94	
95 to 100	
White blood count	3
2000 to 3000	
3000 to 4000	
4000 to 6000	
6000 to 7000	4
7000 to 8000	4
8000 to 9000	5
Sedimentation rat. (mm. per hour)	4
to	
to 5	9
5 to 10	6
10 to 20	
Wassermann and Kahn	
Negative	30
Positive	
Electrocardiograms	
No significant changes	9
Evidence of myocardial damage	3
Basal metabolic rate	
Within normal limits	9
Minors rate	
Röntgenograms of hands	
No bone changes	7
Changes in terminal phalanges	
Sclerodactylia	3
Peripheral circulation	
Functional occlusion only	30
Organic occlusion	
plus	5
plus	3
plus	4
Associated trophic disturbances	
Loss of fingernails	4
Ulcers	5
Loss of tissue	5
Scleroderma	
plus	
plus	3
plus	

the joints, ulcers, loss of tissue, loss of fingernails and sclerodactylia occurred in patients with the most organic vascular pathology as determined by plethysmographic studies. The manner of making these studies has been presented in a previous article (3) but illustrative records will be shown in case reports to follow.

#### TREATMENT

The treatment of patients with Raynaud's symptoms may be classified as follows: (1) the

relief of mental anxiety (2) the improvement of an anemia (3) the treatment of any specific disease, (4) surgical treatment by operations on the sympathetic nervous system.

*The relief of mental anxiety.* Case 4 is striking example. Previous to the onset of the Raynaud's symptoms in December 1936, the patient had been told that she had diabetes. She continued

on a diet until she was admitted to St Luke's Hospital Out Patient Dispensary for care in October, 1937. A thorough examination revealed no evidence of diabetes. About one week after the patient had been reassured she did not have diabetes the Raynaud's symptoms disappeared. Dr Joseph L. Miller communicated to the author the incident of a patient in whom the Raynaud's symptoms disappeared following an auto accident. It is possible the marked emotional change in these patients was sufficient to effect a cure.

*The improvement of an anemia* This is well illustrated by the following report

Mrs L. A., a white female, aged 45 years, first came under observation November 18, 1936, with complaints of typical severe Raynaud's symptoms in the first three fingers of both hands, and similar attacks in the large toes of both feet. The attacks first appeared 3 years previously in the winter and during the cold weather were so severe that she was virtually confined indoors. The symptoms were absent in the summer. She gave a history of severe uterine bleeding during and between menstrual periods. She had been advised to have this treated, but had refused because of fear of an operation. A blood count revealed the red blood cells as 3,910,000 and the hemoglobin as 45 per cent. She still refused surgery, but following intensive liver and iron therapy her blood count improved to within normal limits and as long as maintained she remained virtually free from Raynaud's symptoms even in the winter. She had only one or two attacks per month as compared to several a day before treatment. In the spring of 1939, following a hysterectomy her blood count rose further. On February 22, 1940, her red blood cell count was 5,350,000 and her hemoglobin 115 per cent. She remained free from Raynaud's symptoms the following winter.

Several patients in this series had a similar, but possibly not so striking, improvement as this.

*The treatment of an underlying specific disease* The following illustrates what may be accomplished if the cause of the Raynaud's symptoms can be found.

The patient had severe Raynaud's symptoms since 1932 with associated ulcers, loss of tissue, loss of fingernails

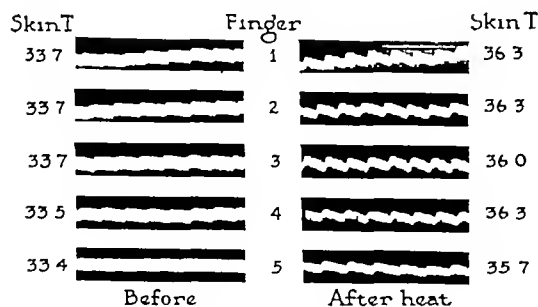


Fig 2 B C The effects of local heat on the skin temperatures and finger volume changes of both hands 22 days following the removal of the right stellate and second dorsal sympathetic ganglia. Note that the skin temperatures

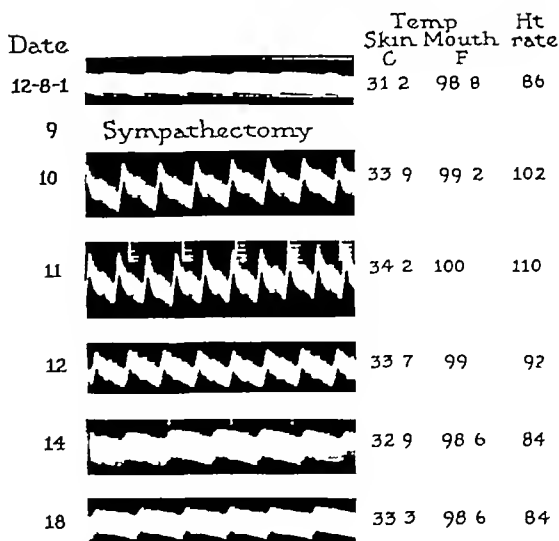
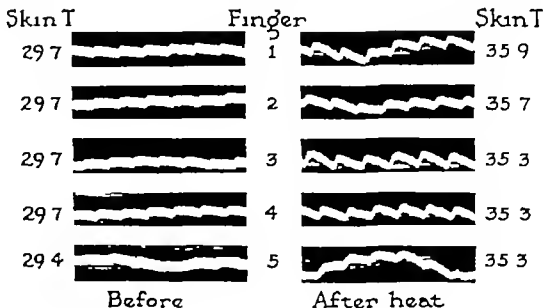


Fig 1 B C The effects of removal of the stellate and second dorsal sympathetic ganglia on the finger volume changes and skin temperatures of the third finger. Note the return of the finger volume changes to the pre-operative level in 21 days in spite of the fact that the skin temperature remained elevated. (From Surg, Gynec & Obst, 1932, Dec)

stiff joints of the fingers, scleroderma and sclerodactylia. In 1934 she was subjected to a bilateral removal of the stellate and second dorsal sympathetic ganglia, with very transient improvement. The symptoms gradually became worse. In June, 1935 antiluetic treatment was instituted. From then on she had complete relief from the Raynaud's symptoms through five winter seasons. Although the Raynaud's symptoms have been relieved completely, she has occasional ulcers on her fingers. Records taken from this patient following surgery are illustrated in Figures 6, 7, and 8.

*Operations of the sympathetic nervous system* In 1932 Johnson, Scupham, and Gilbert published



on the right side are higher than those of the left even though the finger volume changes in both hands are about the same. Also note that local heat produced about the same degree of vasodilatation on both sides.

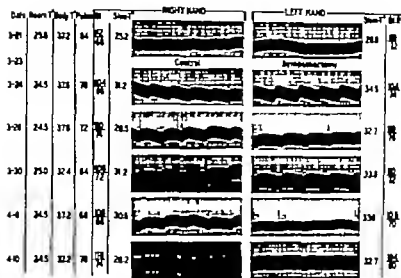


Fig. 3 T A. The effects of removal of the stellate and second dorsal sympathetic ganglia on the body temperature, the skin temperature of the third finger of both hands, the pulse and blood pressures. The right side as used for control. Note that the body temperature and pulse did not change appreciably; that the skin temperatures of the third finger of the left, which as also true of the other fingers, remained elevated above that of the right, and that the finger volume changes increased sooner but immediately follow the operation, but in 8 days returned to their former levels. A similar operation as later done on the right side.

the results of removal of the stellate and second dorsal sympathetic ganglia in one patient and indicated that the peripheral circulation was improved only temporarily in this patient thus confirming earlier experiments by others on animals. For the sake of completeness, a discussion of this first case is included with this report.

The types of operations performed were as follows: (1) unilateral removal of the stellate and second dorsal sympathetic ganglia; (2) bilateral removal of the stellate and second dorsal sympathetic ganglia; (3) bilateral removal of the stellate and third dorsal sympathetic ganglia; (4) bilateral preganglionic section of the sympathetic chain below the third dorsal ganglion; (5) removal of left stellate and second dorsal sympathetic ganglia and right preganglionic section of the sympathetic chain below the third dorsal ganglion.

The results of the studies of these patients are given as follows:

*Unilateral removal of the stellate and second dorsal sympathetic ganglia.* The results of the study of this patient have already been reported, but brief review is included here to show follow up studies and to correlate the findings with those of the 5 patients subsequently operated upon.

B C. This female, aged years at the time of operation as admitted to St. Luke Hospital on August 28, 1930. Her diagnosis of long standing rheumatoid arthritis. The early manifestations of the disease started when she was 25 years of age, but subsided and was not severe until she was 38 years old. At that time, the disease progressed until all the joints except those of the spinal column were in chronic and deformed. Reports in the literature at that time, indicated beneficial results from operations on the sympathetic nervous system. A unilateral removal of the stellate and second dorsal sympathetic ganglia as done by Drs. Carl Hedblom and H. J. Meyer. Studies of the peripheral circulation were made before and at frequent intervals after the operation. No other therapeutic procedures were used for months following the operation so that proper evaluation of any beneficial result from the operation could be made. The patient showed no clinical improvement, but later had considerable improvement from corrective orthopedic procedures.

Figure shows the marked increase of the finger volume changes immediately after the operation. The circulation had returned to the pre-operative level 21 days later although the skin temperatures of the side operated upon remained above those of the control side. Figure illustrates the effects of local heat to the hands before and 21 days after the operation. This record furnishes more proof that the peripheral circulation had returned to the pre-operative

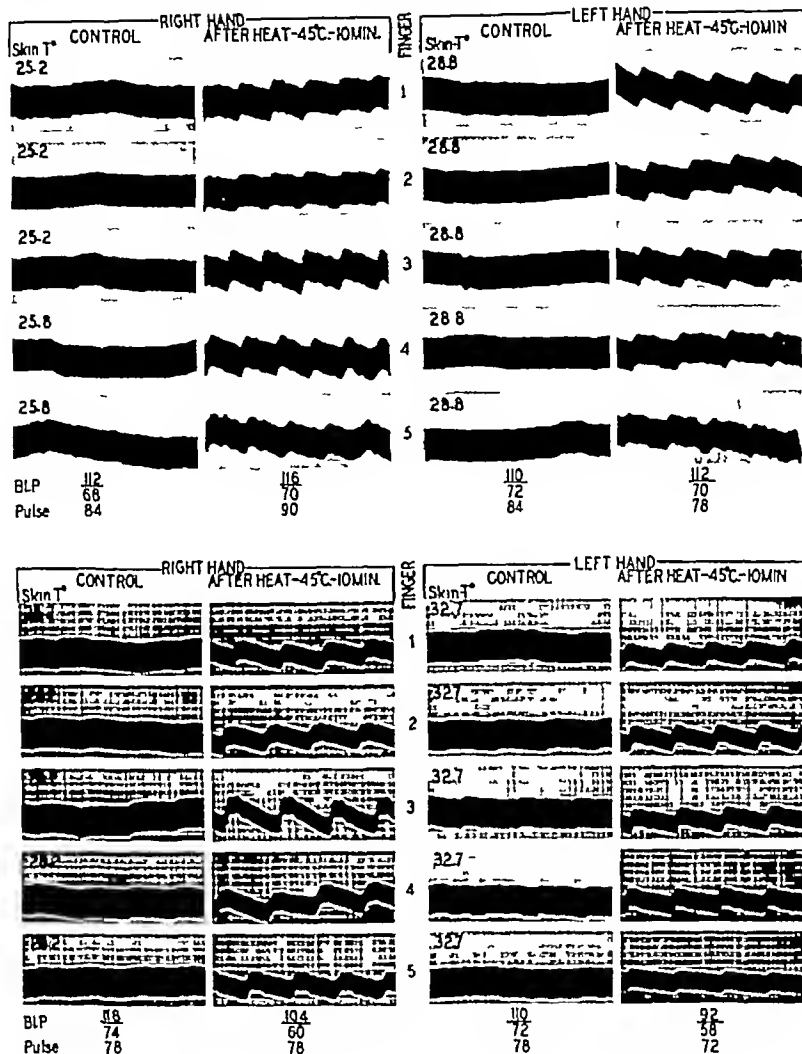


Fig 4 T A The effects of local heat to the hands before, above, and 18 days after below, operation on the blood pressures, the pulse rate, and the finger volume changes. Note that on both occasions the control finger volume changes were abnormally low and local heat caused about the same amount of increase both before and 18 days following operation. The control skin temperatures also were lower than normal. Note also the lack of correlation between the skin temperature and the finger volume changes of the left hand 18 days after operation.

level as local heat caused a vasodilatation similar to that preceding the operation.

Conclusion from this study is that the peripheral circulation returned to its pre operative level within 21 days following the operation. Further conclusions will follow presentation of 5 additional cases.

CASE 1 Bilateral resection of the stellate and second dorsal sympathetic ganglia.

T A, a white female, aged 33 years, was admitted to Passavant Hospital on March 23, 1936, on the service of Dr. Loyal Davis, for surgical relief of Raynaud's symptoms. Since November, 1932, the fingers of both hands had turned white, blue, and red, then normal. At first, only the second and third fingers of both hands had been involved to the second interphalangeal joints, later the second, third, fourth, and fifth fingers of both hands had become involved to the metacarpophalangeal joints. These attacks occurred mainly on exposure to cool air but also to cold water, and during emotional spells as well as following cold



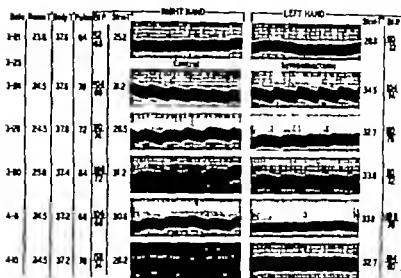


FIG. 3 T A. The effects of removal of the stellate and second dorsal sympathetic ganglion on the body temperature, the skin temperature of the third finger of both hands, the pulse and blood pressure. The right side, as used for control. Not that the body temperature and pulse did not change appreciably; that the skin temperatures of the third finger of the left, which, as also those of the other fingers, remained elevated above that of the right, and that the finger volume changes decreased somewhat immediately following the operation, but in 3 days returned to their former levels. A similar operation, as later done on the right side.

the results of removal of the stellate and second dorsal sympathetic ganglia in one patient and indicated that the peripheral circulation was improved only temporarily in this patient, thus confirming earlier experiments by others on animals. For the sake of completeness, a discussion of this first case is included with this report.

The types of operations performed were as follows: (1) unilateral removal of the stellate and second dorsal sympathetic ganglia, (2) bilateral removal of the stellate and second dorsal sympathetic ganglia, 3 cases (3) bilateral removal of the stellate and third dorsal sympathetic ganglia (4) bilateral preganglionic section of the sympathetic chain below the third dorsal ganglion, (5) removal of left stellate and second dorsal sympathetic ganglia and right preganglionic section of the sympathetic chain below the third dorsal ganglion.

The results of the studies of these patients are given as follows:

1. *Unilateral removal of the stellate and second dorsal sympathetic ganglia.* The results of the study of this patient have already been reported, but brief review is included here to show follow-up studies and to correlate the findings with those of the 5 patients subsequently operated upon.

B. C. H. female, aged 35 years at the time of operation, as admitted to St. Luke's Hospital on August 26, 1930, with diagnosis of long standing rheumatoid arthritis. The early manifestations of the disease started when she was 25 years of age, but subsided and were not severe until she was 33 years old. 1 year of treatment, the disease progressed until all the joints except those of the spinal column were involved and deformed. Reports in the literature at that time indicated beneficial results from operations on the sympathetic nervous system. A unilateral removal of the stellate and second dorsal sympathetic ganglia, as done by Drs. Carl Hertzblom and H. J. Meyer. Studies of the peripheral circulation were made before and at frequent intervals after the operation. No other therapeutic procedures are used for months following the operation so that proper evaluation of any beneficial result from the operation could be made. The patient showed no clinical improvement, but later had considerable improvement from corrective orthopedic procedures.

Figure 1 shows the marked increase of the finger volume changes immediately after the operation. The circulation had returned to the pre-operative level 2 days later although the skin temperatures of the side operated upon remained above those of the control side. Figure 2 illustrates the effects of local heat to the hands before and 4 days after the operation. This record furnishes more proof that the peripheral circulation had returned to the pre-operative

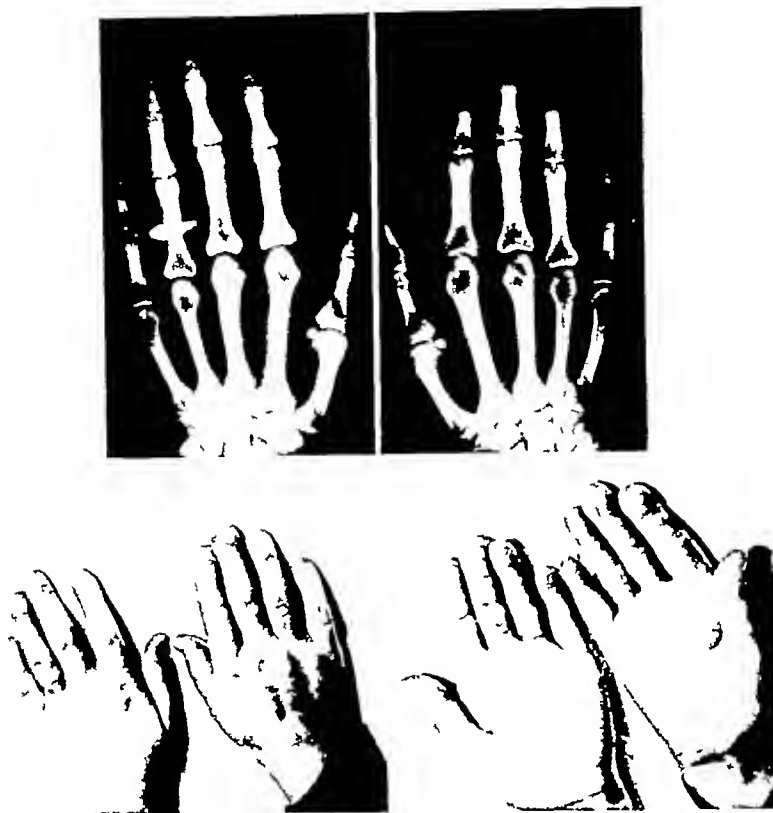


Fig 6 M.B. Above, roentgenograms of the hands illustrating the sclerodactylia and bony changes in the terminal phalanges. Below, photographs of the hands showing scleroderma, changes in the fingernails, and loss of tissue on the ends of the fingers.

tion and at frequent intervals subsequently. A similar operation was done on the right side at a later date.

Measurements of the peripheral circulation were made before and daily after the operation until the finger volume changes had reached the pre-operative level in 16 days as compared with 21 days in the previous case (Fig 3). Here, too, the skin temperatures remained higher on the side operated upon. Figure 4 shows the vasodilating effects of heat before and 18 days following the left sympathectomy. The records are similar, indicating that the vessels had regained their pre-operative tone.

Figure 5 shows the effects which were produced by median nerve block on the finger volume changes before and 17 days following the left sympathectomy. Although the characteristic numbness occurred in the first three fingers of the left hand, there was no evidence of vasodilatation. This is offered as proof of the completeness of the operation.

#### CASE 2 Bilateral removal of stellate and second thoracic sympathetic ganglia

M.B. white female, aged 47 years. I first saw her March 13, 1935 because of Raynaud's symptoms which had been present since the winter of 1930. All her fingers turned white to the metacarpophalangeal joints. They then turned blue, red, and back to normal. She did not remember having frozen the fingers. These attacks continued and became more severe in frequency and duration. In the winter they necessitated staying indoors virtually all the time, even then she had two to three attacks daily. The attacks were caused most easily by cool air, less so by cool water. She remembered only one attack associated with an emotional upset. The attacks were relieved most easily by immersion of the hands in cold water, followed by warm water. The patient had numerous trophic disturbances and since 1931 had lost fingernails from the first, second, and third fingers of both hands. The past history was negative except for typhoid at 8 years, a rectal fistula at 25 years, and influenza at 30 years. Examination was essentially negative except for evidence of loss of tissue on the tips of the fingers, disturbance of growth of the fingernails, scleroderma, stiffness of the finger joints, and sclerodactylia (Fig 6). Dr Loyd Davis did a bilateral removal of the stellate and second thoracic sympathetic ganglia in January, 1934. For a time the patient thought she had improved, particularly as the warm weather set in. The

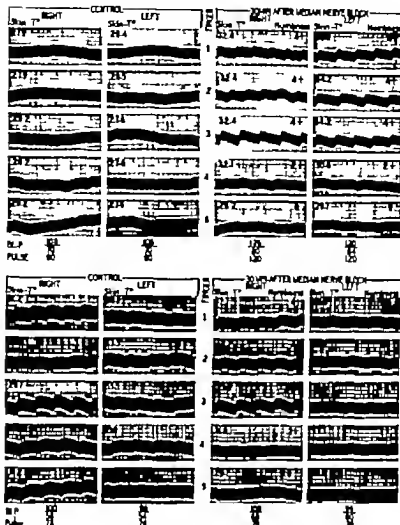


Fig 5 T.V. The effects of median nerve block at the wrist on the blood pressure, pulse rate and finger volume changes of both hands before, above, and, below, 7 days following removal of left stellate and second dorsal sympathetic ganglia. Note that before the operation the median nerve block produced an increase of the finger volume changes and increased skin temperature of the first three fingers and less so in the fourth, little in the fifth finger there was no change. Following operation, satisfactory test could not be made because the patient became emotionally unstable. Even though satisfactory nerve block as obtained as evidenced by the numbness, the finger volume changes did not become increased.

drinks, ice cream, or chilling of the body. The attacks are more frequent and severe in winter but occurred in the summer too. There is some pain in the fingers during the white and blue stages and numbness during the red stage, which disappeared on recovery. The attacks are relieved by rubbing the hands together. No trophic disturbances are present except an ulcer on the second right finger which started in 1935 and still pains her but no pus was present. She has several attacks per day which last from 5 to 15 minutes. The past history is negative.

The physical examination is negative except for the stubby appearance of the fingers. All the peripheral vessels are easily palpable. The patient is noticeably unstable emotionally and during vascular studies had hysterical attacks which sometimes lasted an hour. The laboratory findings are negative except for a basal metabolic rate. Dr. Davis removed the left stellate and second dorsal sympathetic ganglia on March 5, 1936. The right arm was studied as control. It is interesting to note that symptoms recurred 8 days following the opera-

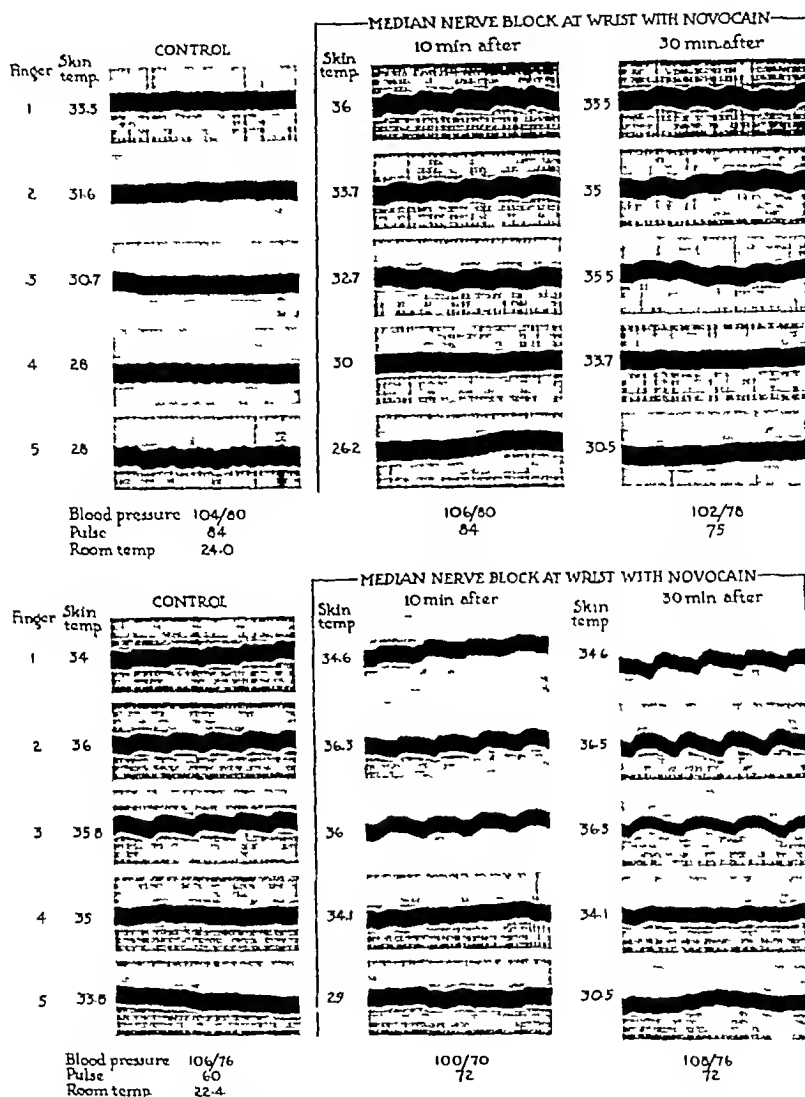


Fig 8 M B The effects of median nerve block on the finger volume changes, skin temperature of the fingers, pulse rate, and blood pressure. Note the moderate vasodilating effect of this procedure in the first 3 fingers of both hands as well as an increased skin temperature in these fingers. The finger volume changes of the fourth and fifth fingers did not change. In the fourth and fifth fingers of the right hand, below, the skin temperatures decreased, which is the usual finding in normal individuals from this procedure. Above, left hand record.

release of the vasospasm, even though theoretically, this should not occur following extensive surgery on the sympathetic nervous system. Three winters have elapsed since the operation. The Raynaud's symptoms are as severe as before the operation.

**CASE 4** Bilateral pre ganglionic section of the sympathetic chain below the third dorsal ganglion.

Mr Y, white male, aged 47 years, was first seen on May 25, 1937, for Raynaud's symptoms. In 1932 he noticed

that all the fingers turned white to the metacarpal phalangeal joints, then passed through the various stages of blue, red, then normal. The symptoms had their onset in the toes also at the same time as in the fingers. They were brought on most easily by cool air, chilling of the body, or during emotional attacks, but were not affected by cold drinks. During the attacks he occasionally fainted. The Raynaud's symptoms lasted from a very short time to several hours, when nothing seemed to relieve them. The



Fig. 7. S.B. The effects of local heat on the finger volume changes. Note the absence of pulsatile changes in the control records as well as no appreciable vasodilating effect of local heat particularly in the left hand, above. Bilateral removal of the stellate and second thoracic sympathetic ganglia had been done about 4 months before these records were made. Below right hand record.

following. Inter the symptoms were as severe, or more so, than before the operation. The symptoms continued to progress in severity and duration and caused ulcers beyond the first interphalangeal joints. In June, 1936, treatment for an old syphilis was started. Since that time she has had complete relief of the Raynaud's symptoms although ulcers still occur on the fingers. The scleroderma has improved.

Studies of the peripheral circulation were made in the fall of 1935. Figure 7 shows the effects of local heat on the peripheral pulse volume changes. The small response before and after heat indicates marked organic changes in the peripheral vessels,

especially in the left hand. Figure 8 shows the effects of median nerve block on the finger volume changes. This procedure produced an improvement of the circulation in fingers innervated by the median nerve. The operation should have destroyed the vasomotor fibers traveling in the median nerve. It is difficult to understand this result unless some vasomotor fibers still remained, or somatic motor fibers may be partly vasomotor in function. The patient does not perspire in the hands or arms. It does not seem likely, however, that regeneration of the vasomotor fibers would occur without regeneration of the sweat fibers.

This case is particularly instructive because it illustrates the inadequacy of our knowledge of the sympathetic nervous system as well as the pathogenesis of Raynaud's symptoms.

#### CASE 5. Bilateral removal of the stellate and third sympathetic ganglia

D. L., white female, aged 49 years, as admitted to Massachusetts Hospital April 8, 1938, as patient of Dr. Loyal Davis, for the surgical relief of Raynaud's symptoms. She complained that for the past 3 years her fingers had turned successively white, blue, dark red, then back to normal. Similar symptoms did not occur in the toes. Three attacks were brought on most easily by emotional spells, exposure of the hands to cold air, cool water after clothing of the body and after she drank cold drinks and ate cold foods. There was numbness but no pain during these symptoms. The attacks could occur most frequently at the water but some took place in the summer too. They are relieved by immersion of the hands in warm water. If this were not done the attacks lasted until she overcame her emotional spell. The past history was negative except for attacks of migraine which began at the age of 6 years and continued until she was 45 years. The menopause occurred at the age of 45 years.

The physical examination was essentially negative. Roentgenograms of the chest and an electrocardiogram showed normal records. The results of the laboratory examinations are shown in Table II. The radial, ulnar, dorsalis pedis, and posterior tibial arteries were easily palpable.

The pre-operative studies on the peripheral circulation are illustrated in Figures 9 and 10. The vessels of the fingers are spastic and the plethysmographic records showed little or no pulsations. This was relieved by the application of local heat. The vessels are spastic at the time the effects of the median nerve block are being measured. Although block as produced by the characteristic numbness of the first three fingers of both hands, relief of the spasm did not occur. This is difficult to explain as there is only one other patient who has median nerve block failed to relieve functional spasm of the vessels to the first three fingers.

On April 20, 1938, Dr. Davis resected the stellate and third dorsal sympathetic ganglia from which the patient made an uneventful recovery. Measurements of the peripheral circulation were repeated after operation. The effects of local heat are measured on June 1, 1938, by similar procedures. The results, as shown by Figure 9, indicated the vessels are more spastic than before the operation. The Raynaud's symptoms had recurred. The effects of median nerve block are measured on October 5, 1938, and at this time (Fig. 10) as possible to obtain

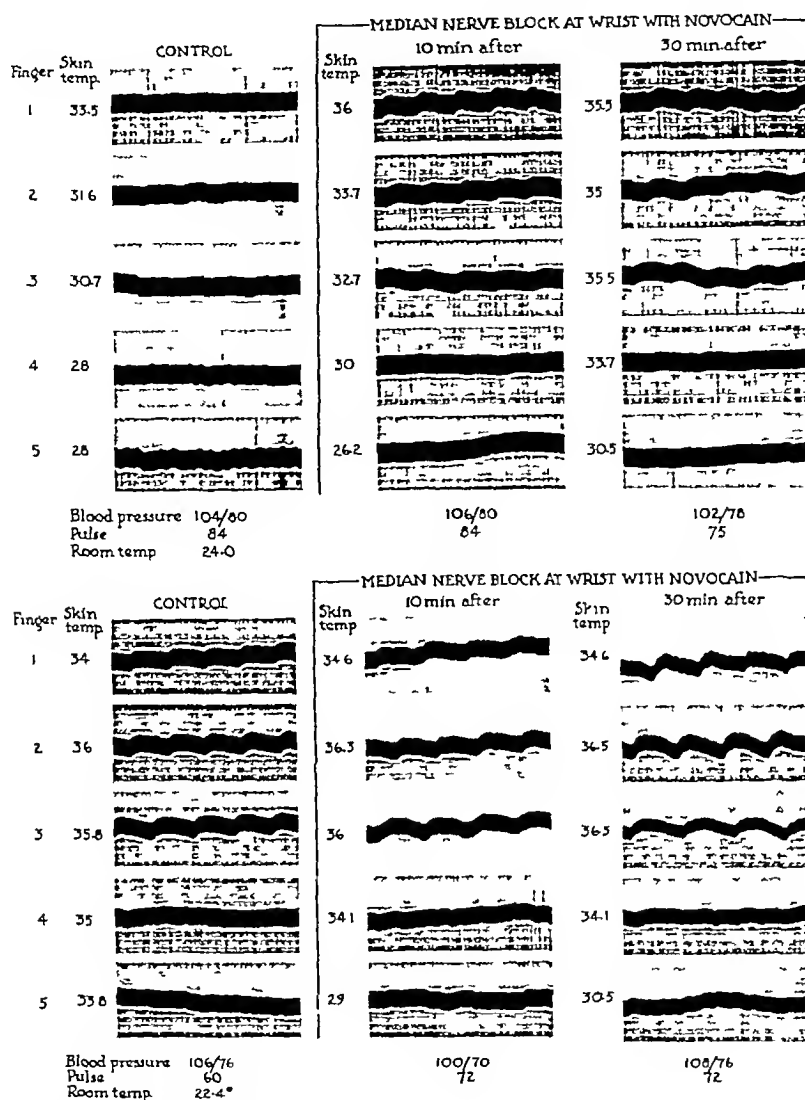


Fig. 8 M B The effects of median nerve block on the finger volume changes, skin temperature of the fingers, pulse rate, and blood pressure. Note the moderate vasodilating effect of this procedure in the first 3 fingers of both hands as well as an increased skin temperature in these fingers. The finger volume changes of the fourth and fifth fingers did not change. In the fourth and fifth fingers of the right hand, below, the skin temperatures decreased, which is the usual finding in normal individuals from this procedure. Above, left hand record.

release of the vasospasm, even though theoretically, this should not occur following extensive surgery on the sympathetic nervous system. Three winters have elapsed since the operation. The Raynaud's symptoms are as severe as before the operation.

CASE 4. Bilateral pre ganglionic section of the sympathetic chain below the third dorsal ganglion.

Mr. Y, white male, aged 47 years, was first seen on May 25, 1937, for Raynaud's symptoms. In 1932 he noticed

that all the fingers turned white to the metacarpal phalangeal joints, then passed through the various stages of blue, red, then normal. The symptoms had their onset in the toes also at the same time as in the fingers. They were brought on most easily by cool air, chilling of the body, or during emotional attacks, but were not affected by cold drinks. During the attacks he occasionally fainted. The Raynaud's symptoms lasted from a very short time to several hours, when nothing seemed to relieve them. The

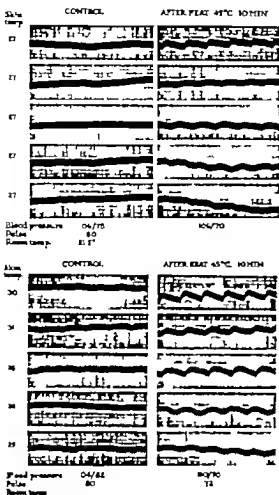


Fig. 7. ALB. The effects of local heat on the finger volume changes. Note the absence of pulsatile changes in the control records as well as no appreciable vasodilating effect of local heat particularly in the left hand, above. Bilateral removal of the stellate and second thoracic sympathetic ganglia had been done about 4 months before these records are made. Below, right hand record.

following winter the symptoms are as severe, or more so, than before the operation. The symptoms continued to progress in severity and duration and crested ulcers beyond the first interphalangeal joints. In June, 1936, treatment for an old syphilis was started. Since that time she has had complete relief of the Raynaud's symptoms although ulcers still occur on the fingers. The scleroderma has improved.

Studies of the peripheral circulation were made in the fall of 1935. Figure 7 shows the effects of local heat on the peripheral pulse volume changes. The small response before and after heat indicates marked organic changes in the peripheral vessels,

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This case is particularly instructive because it illustrates the inadequacy of our knowledge of the sympathetic nervous system as well as the pathogenesis of Raynaud's symptoms.

#### CASE 3. Bilateral removal of the stellate and third sympathetic ganglia.

D. L., Miss female, aged 40 years, was admitted to Passaic Hospital April 8, 1938, as patient of Dr. Lloyd Davis, for the surgical relief of Raynaud's symptoms. She complained that for the past 3 years her fingers had turned successively blue, blue, dark red, then back to normal. Similar symptoms did not occur in the toes. These attacks were brought on most easily by emotional spells, exposure of the hands to mild cold air, cooler chilling of the body and after she drank cold drinks and ate cold foods. There are numbness but no pain during these symptoms. The attacks could occur most frequently in the winter but some took place in the summer too. They were relieved by immersion of the hands in warm water. If this is not done, the attacks lasted until she overcame her emotional spell. The past history is negative except for attacks of migraine which began at the age of 6 years and continued until she was 45 years. The menopause occurred at the age of 45 years.

The physical examination was essentially negative. Roentgenograms of the chest and an electrocardiogram showed normal records. The results of the laboratory examinations are shown in Table II. The radial, ulnar, dorsalis pedis, and posterior tibial arteries are easily palpable.

The pre-operative studies on the peripheral circulation are illustrated in Figures 9 and 10. The vessels of the fingers are spastic and the plethysmographic records show little or no pulsations. This is relieved by the application of local heat. The vessels are spastic at the time the effects of the median nerve block are being measured. Although block as produced with the characteristic numbness of the first three fingers of both hands, relief of the spasm did not occur. This is difficult to explain as there is only one other patient in whom median nerve block failed to relieve functional spasm of the vessels to the first three fingers.

On April 30, 1938, Dr. Davis resected the stellate and third dorsal sympathetic ganglia from which the patient made an uneventful recovery. Measurements of the peripheral circulation are repeated after operation. The effects of local heat are measured on June 1, 1938, by similar procedures. The results, as shown by Figure 9, indicated the vessels are more spastic than before the operation. The Raynaud's symptoms had returned. The effects of median nerve block are measured on October 5, 1938, and at this time (Fig. 10) it is possible to obtain

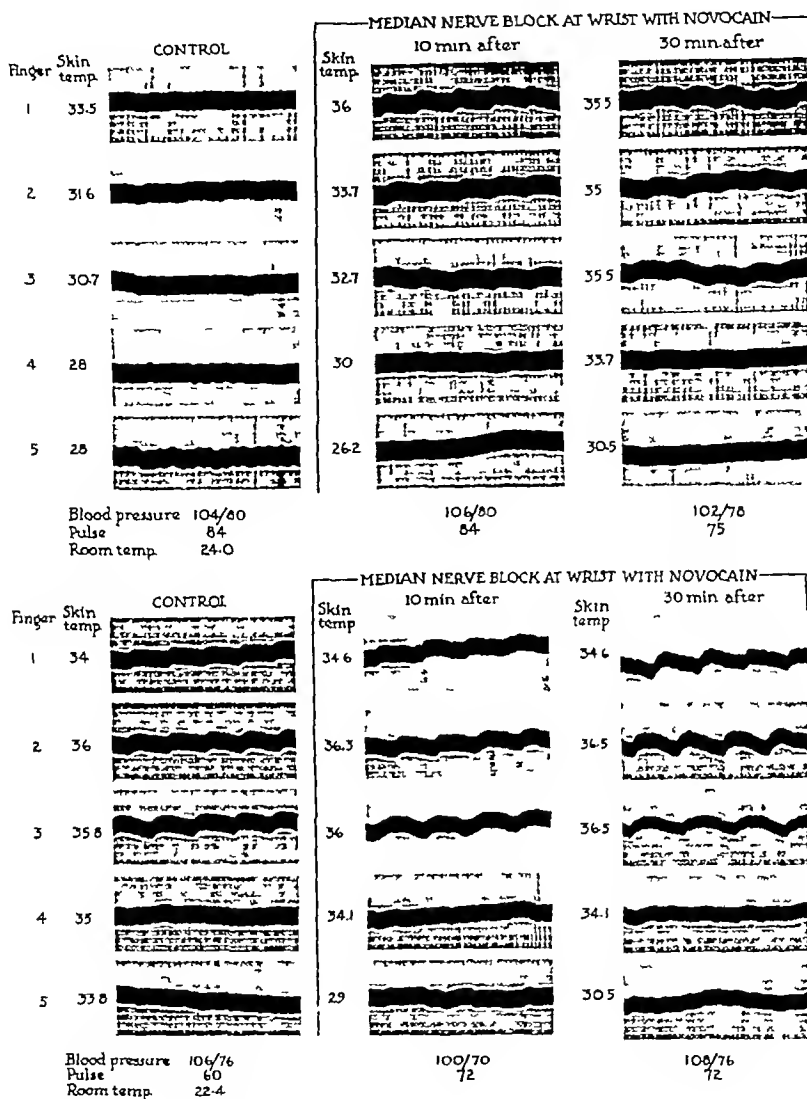


Fig 8 MB The effects of median nerve block on the finger volume changes, skin temperature of the fingers, pulse rate, and blood pressure. Note the moderate vasodilating effect of this procedure in the first 3 fingers of both hands as well as an increased skin temperature in these fingers. The finger volume changes of the fourth and fifth fingers did not change. In the fourth and fifth fingers of the right hand, below, the skin temperatures decreased, which is the usual finding in normal individuals from this procedure. Above, left hand record.

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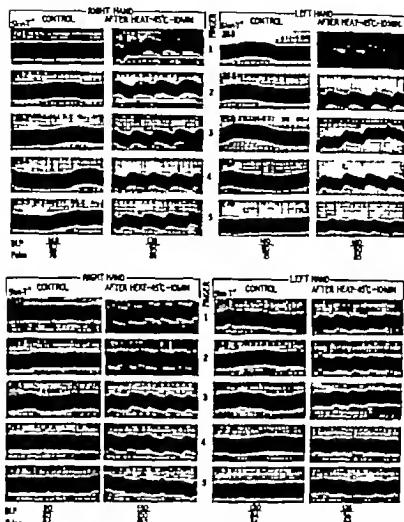


Fig. 9. D.L. The effects of local heat to the hands on the finger volume changes before and 63 days following the bilateral removal of the stellate and third dorsal sympathetic ganglia. Note the absence of pulse volume changes in the controls both before above, and after below the sympathectomy in spite of the increased skin temperature following the operation. The local heat produced about the same amount of vasodilatation before and after the operation.

attacks usually were relieved by immersion of the hands in warm water after shaking of the hands, or exercise. The condition was more intermittent and comparatively absent during the summer.

In February 1936, bilateral lumbar sympathectomy was done at the Hines Hospital by Dr. Da la. This changed the character, but not the severity of the symptoms. The toes no longer turned white, but the stinging sensation in the toes persisted. The most distressing symptoms had occurred since the operation were profuse night sweats of the legs followed by sensation of extreme cold to the touch. The physical examination was essentially negative except for reference to the extremities.

The radial, ulnar, posterior tibial, and dorsalis pedis arteries palpated normally. Studies are made of the peripheral circulation (Figs. 2, 3, and 4). These results indicate there is no significant organic pathology in the peripheral vessels.

On June 1937 Dr. Da la did bilateral preganglionic section of the sympathetic chain below the third dorsal ganglia according to the method described by Smithwick. Detailed postoperative studies of the peripheral circulation are made (Fig. 5). These results show that peripheral circulation had returned to pre-operative level in about 6 days. It is interesting to note that the sweating reaction in the arms and hands had returned in about 6 days.

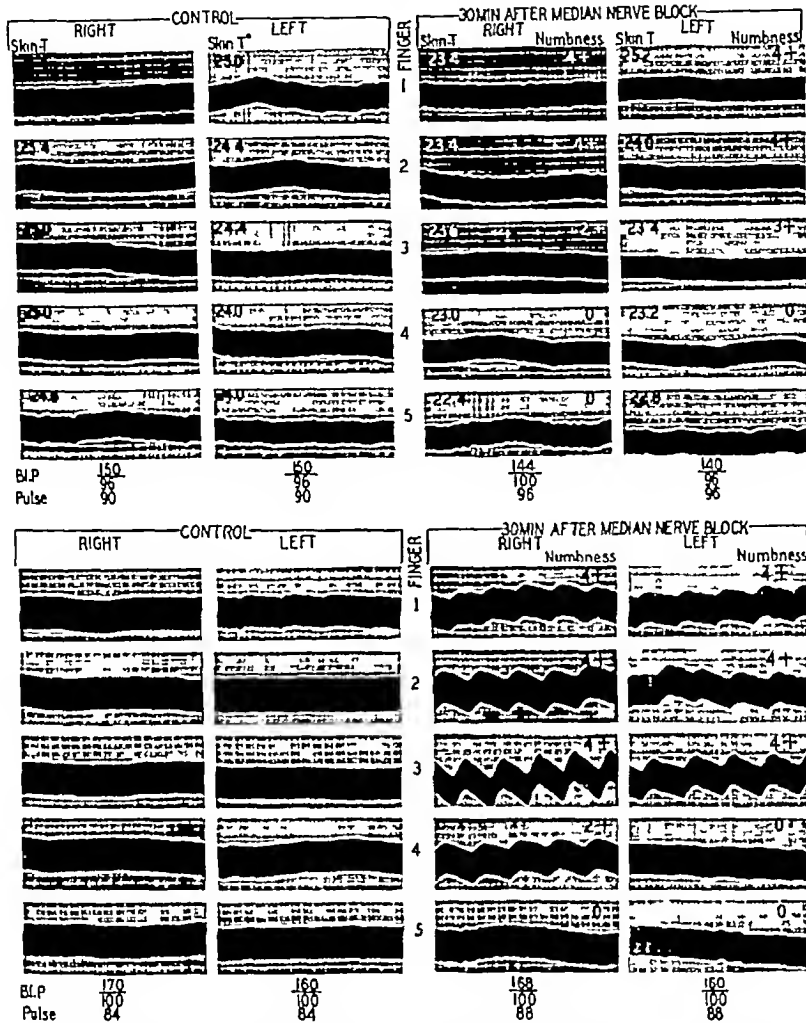


Fig 10 DL The effects of median nerve block with novocain at the wrist on the finger volume changes before, above, and, below, 168 days following a bilateral removal of the stellate and third dorsal sympathetic ganglia. Following the injection of novocain during the experiment as illustrated in the upper record, the patient felt faint and a severe attack of Raynaud's symptoms occurred in spite of a good nerve block as illustrated by the characteristic numbness in the first three fingers. Note the absence of pulse volume changes in both the control and after median nerve block in the upper record, the low skin temperatures before and after nerve block which is not the normal response in the first three fingers. The patient had typical Raynaud's symptoms during nerve block in the first three fingers of each hand. In the lower record there is an absence of finger volume changes in the control records. Following median nerve block, vasodilatation occurred in the fingers innervated by the median nerve, in the apparent absence of sympathetic vasomotor nerves. The patient had a persistent absence of sweating in the upper extremities indicating the completeness of the operation. The median nerve block induced a Raynaud's attack in the fifth fingers, apparently from diversion of blood to the other fingers.

The effects of local heat were measured before and 12 days after operation, and of the median nerve block before and 14 days after operation (Figs 12 and 13). The results indicate that the peripheral vessels were able to dilate fol-

lowing the operation just as before, indicating the circulation had returned to the pre-operative level. Beneficial effects of the operation were only transitory for the symptoms recurred within 1 month and continued to be as severe

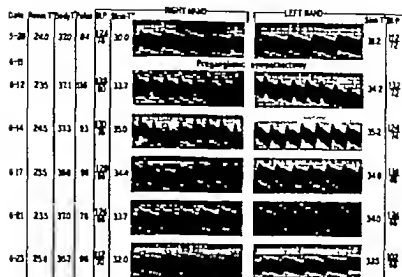


Fig. 1. The effects of the preganglionic type of sympathetic operation in which the sympathetic chain is severed below the third thoracic on both sides. Note that there are no changes, vascular or otherwise which persisted beyond the traumatic effects of the surgery.

or more so than before. He now has intractable headaches associated with the Raynaud' symptoms and often faints. Last winter an attack of Raynaud' symptoms lasted about 4 hours and could not be relieved by the usual methods.

It is interesting to note that his 6 year old son now has occasional attacks of Raynaud' symptoms.

The results in this case indicate the inadequacy of surgical procedure for the relief of the patient's symptoms.

**CASE 5.** Removal of left stellate and second dorsal sympathetic ganglia and right preganglionic section of the sympathetic chain below the third dorsal ganglion.

H. H. White female, aged 36 years, as admitted to Pennant Hospital on the service of Dr. Loyd Davis for surgical relief of Raynaud' symptoms. Her complaints are that all of her fingers turned white, then blue, red, and then finally normal. She had frequent headaches, dizziness, and congestion, and soreness in the eyes. The attacks of Raynaud' symptoms began in her hands and feet at the same time about 8 years previously. She did not know whether the attacks were more in the hands or feet, but her attention was drawn mostly to her hands. Here the attacks were brought on most easily by exposure to cool air, less so by emotional spells, and less so by immersion of the hands in cold water. They were relieved most easily by exposure to warm air and water and would even stop spontaneously. The attacks necessitated staying indoors during the cold, either but could occur frequently in summer too.

No pain accompanied the attacks, but during the white stage the fingers felt cool and numb. Recovery with warm air left no further subjective symptoms. On the other hand, when the hands were placed in warm water produced sensation of pins and needles in the fingers.

Physical examination was essentially negative except that the hands appeared swollen. The peripheral vessels were easily palpable and pulsating. The results of laboratory studies are reported in detail in Table II. The slower vital findings are sedimentation rate 14, basal metabolic rate, - 8 and mild secondary anemia.

Studies of the peripheral circulation by means of the digital plethysmograph showed that the effects of local heat and median nerve block before operation were moderate organic changes in the peripheral vessels.

On July 30, 1935, the stellate and second dorsal sympathetic ganglia were removed on the left side while on the right preganglionic section was done according to the method of Smithwick.

Studies of the peripheral circulation were made daily following the operation until the circulation had reached its pre-operative level 8 days later (Fig. 4). The effects of local heat on the finger volume changes were measured days after operation and are similar to the pre-operative records (Fig. 5). The effects of median nerve block also were measured 30 days after operation and, just as before the operation, the nerve block did not relieve the spasm in the fingers although the characteristic numbness occurred following the block. These results are similar to those of Case D. L.

#### ANALYSIS OF STUDY

The symptom complex now known as Raynaud's disease is very little understood in spite of the tremendous amount of study it has received since the original publications of Raynaud. The main reasons for this apparent lack of progress in our knowledge are (1) opinion differs as to whether Raynaud's disease exists as a clinical entity (2) the nature of the vascular changes are

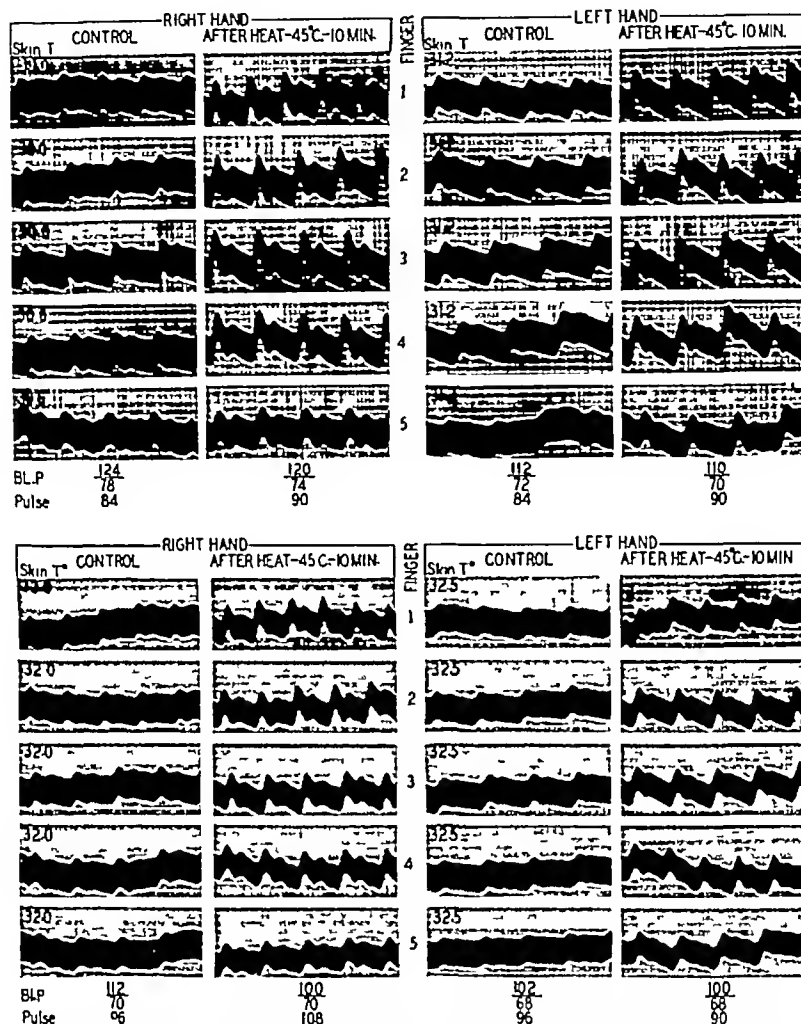


Fig 12 Y The records show the effects of local heat on the finger volume changes before, above, and below, 12 days following the operation and one notes that about the same degree of vasodilatation is induced on both occasions

not understood, and (3) opinion differs regarding treatment. This discussion is based on a study of the 22 patients reported in this article.

*A Does Raynaud's disease exist as a clinical entity?* This answer is of fundamental importance, for it not only forms a common ground for the study of the symptom complex, but also would tend to rationalize understanding of the nature of the vascular changes, as well as the treatment of the symptom complex.

Hutchinson, more than 50 years ago, concluded that what is known as Raynaud's disease does not exist as a clinical entity and the peripheral mani-

festations observed are merely symptoms of some more fundamental disease. Hunt, in a more recent review of the subject, came to essentially the same conclusions and added that if Raynaud's disease exists at all, it must be very rare. He had no solution for a change in terminology. He believes that the term "Raynaud's disease" has such common usage it is doubtful it could be replaced by a more accurate descriptive term, such as Raynaud's syndrome.

The author arrives at the same conclusions from a study of the patients reported in this series, but is aware that persons examining these

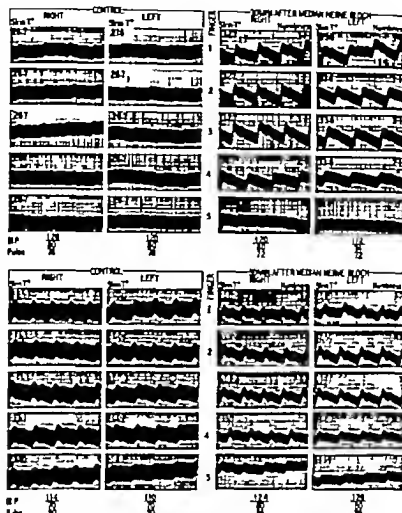


Fig. 1. A The effects of median nerve block 1 hr. just before above, and 4 days after, below, operation mentioned in the legend under Figure. Note that it is possible to produce vasodilatation in the fingers innervated by the median nerve both before and after the surgery.

reports may doubt the accuracy of the diagnosis in many of the patients, as has occurred with Raynaud's original series. Certain data in these studies, however, throw light on the nature of the vascular changes during Raynaud's attacks and further bear out the opinion that the changes observed in the extremities of patients with Raynaud's attacks are merely symptoms of some more fundamental disease.

*B. The nature of the vascular changes in Raynaud's syndrome.* The generally accepted view is that the blanching of the fingers or toes during Raynaud's attack is caused by an active peripheral

vascular constriction. The results of these studies indicate this may not be strictly so.

It is conceivable that the symptom complex in the fingers during a Raynaud's attack may be caused, in part, by a vasodilatation in the palmar arch and a passive collapse of the vessels in the fingers from an inadequate amount of the blood and blood pressure to keep them open. In other words, the blood may be shunted into the palmar arch without going through the fingers. The data in support of these ideas are as follows:

During a Raynaud's attack it has been widely observed that radial pulse does not change

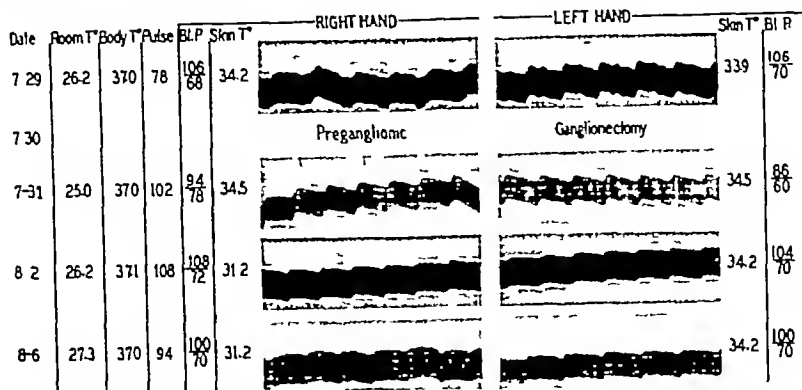


Fig 14 H H The effects of a preganglionic type of operation on the right side and removal of the stellate and second dorsal sympathetic ganglia on the left side on the body temperature, skin temperature, blood pressure, pulse, and finger volume changes. Note that the finger volume changes returned to the pre operative level within 8 days, and that the skin temperature on the right side went below the control level while on the left it remained above the control level.

2 Blood can be diverted from the fingers in a normal individual by the administration of amyl nitrite, as shown in 1932 (3). A vasodilator drug which produces a vasodilatation in one place may produce a *passive* vasoconstriction in another if it causes sufficient diversion of blood to one area with a further resulting fall in blood pressure. In this particular case the amyl nitrite causes a diversion of the blood to the splanchnic area and a fall in blood pressure with insufficient blood and blood pressure to keep the finger vessels open. A similar phenomenon may exist in Raynaud's syndrome as a result of diversion of blood through the palmar arch.

3 One of the effects of median nerve block at the wrist and increased skin temperature is a vasodilatation in the first three fingers, less in the fourth finger, and a decrease in the fifth finger with a fall in skin temperature. The decrease in the circulation in the fifth finger from this procedure is caused by a diversion of blood to allow more blood to pass into the first three fingers. In patients with Raynaud's syndrome the same changes occur. A typical Raynaud's attack frequently occurs in the fifth finger alone. The most apparent explanation for this is that blood diverted from the fifth finger produces a Raynaud's attack, and not an active vascular constriction.

4 In patients with Raynaud's syndrome during periods of freedom from attack, measurements of the circulation of the fingers show a circulation less than normal even in the absence of any organic vascular changes. Under such circumstances it would seem logical to conclude that it would not require as much diversion of blood

to produce a Raynaud's attack as it would in a normal individual. The average amount of blood received by the five fingers under normal conditions is approximately 3.6 cubic centimeters of blood in one minute. In many patients with Raynaud's disease reported in this series, between attacks and under similar environmental conditions, the amount was far less, and measurements indicated that the amounts varied from less than 1 cubic centimeter per minute to the normal 3.6 cubic centimeters.

5 Patients with organic vascular changes who have Raynaud's syndrome suffer more distress from the attacks. It may be that even a lesser diversion of blood from the fingers can produce a Raynaud's attack.

6 If the lesser diversion of blood from the fingers can produce a Raynaud's attack, one cannot expect surgical removal of the vasoconstrictor fibers to the extremity to eliminate the attacks. This is shown by the poor results in 5 patients of this series.

7 Finally, there is so little direct evidence that the sympathetic nervous system is at fault in patients with Raynaud's syndrome, and considerable evidence that the humeral mechanism of peripheral vascular control may be impaired. Further study is indicated in this direction. The evidence of the importance of changes in the blood inducing Raynaud's attacks will be discussed in more detail under "The Treatment of Raynaud's Syndrome."

C The association of other diseases with Raynaud's syndrome. Other conditions or diseases are common with Raynaud's syndrome. In these

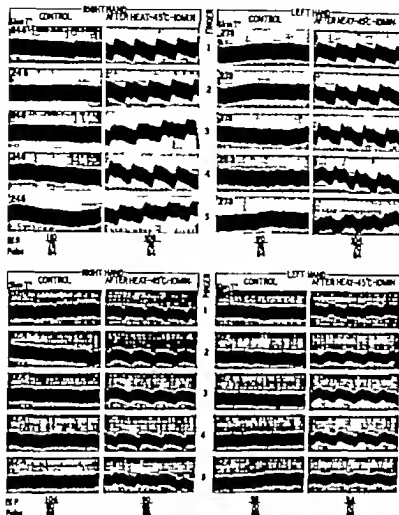


Fig. 5 HIL. The effects of local heat to the hands before, above, and so days following, below operation on sympathetic ganglia. Note the very low amplitude of the finger volume changes in the control records both before and after surgery and that finger volume changes are increased by the application of local heat in both cases.

series the following were found ( ) secondary anemia—mild, 3 cases severe, 2 cases (3) syphilis, cases (3) organic vascular disease—peripheral vascular, 8 cases cardiovascular 3 cases (4) trophic disturbances—ulcers on fingers, 5 cases stiff finger joints, 5 cases loss of finger nails, 4 cases skin, scleroderma, 5 cases bones, sclerodactylia, 3 cases.

This common association with other diseases immediately presents two questions ( ) How much does secondary anemia or syphilis contribute to Raynaud's symptoms? ( ) Do the Raynaud's symptoms lead to organic vascular changes

and trophic disturbances or do they have a common etiology with these changes.

These questions can only partially be answered from observations of patients in this series. As to the first, the treatment of a mild or severe anemia resulted in improvement in all. The degree of improvement varied from slight to almost complete relief from attacks. Syphilis is occasionally associated with Raynaud's symptoms, and was present in 2 patients in this series. The effects of antiluetic treatment could not be observed in one of these patients because he did not stay under observation. In the other who also

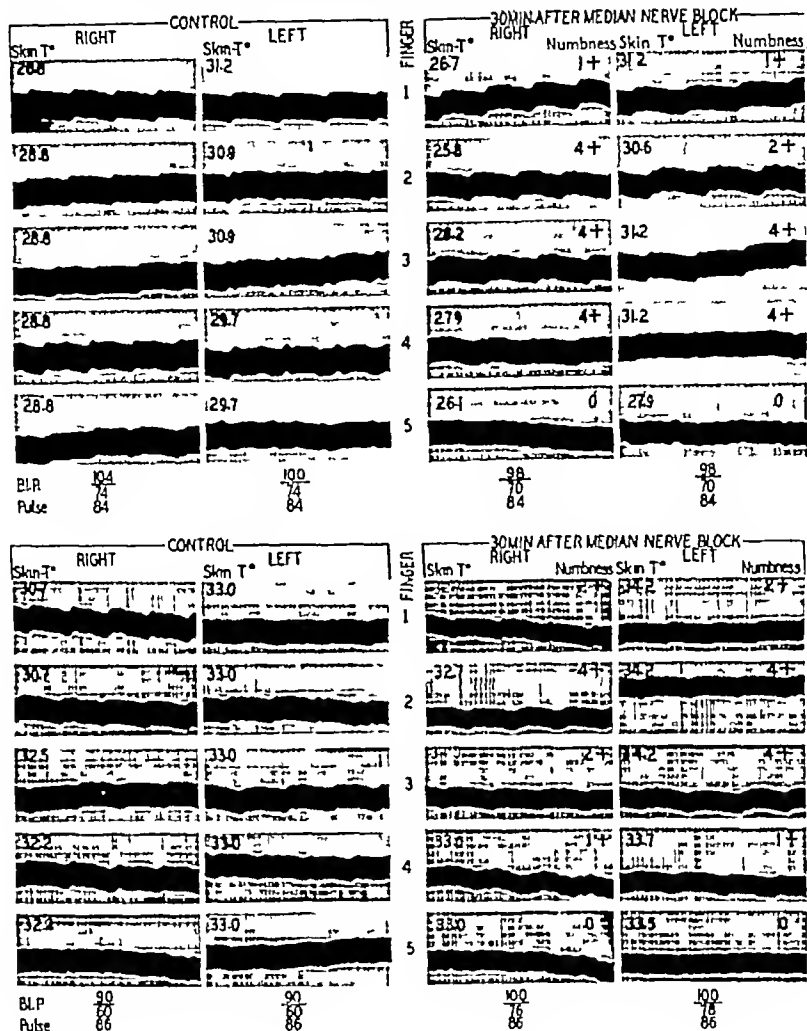


Fig 16 HH The effects of median nerve block at the wrist before, above, and below, 39 days following operation on the sympathetic ganglia. Note that the block did not produce the characteristic increase in finger volume changes in the fingers innervated by the median nerve, either before or after surgery, that the patient did experience the characteristic numbness in the fingers following the block, that the skin temperatures did not change appreciably, and showed no definite correlation with the finger volume changes and that injection of the median nerve induced a typical Raynaud's attack during the course of the experiment as illustrated by the upper record.

had scleroderma and sclerodactylia, complete relief from the Raynaud's symptoms and great improvement of the scleroderma followed anti-luetic treatment. Here a common etiology for the Raynaud's syndrome and the associated diseases is suggested. Organic vascular disease, present in a number of patients, varies from mild organic peripheral changes to severe cardiovascular disease with decompensation. One must

ask (1) How much of the organic changes are secondary to the Raynaud's symptoms? (2) Are the Raynaud's symptoms secondary to the organic vascular changes? (3) Do the Raynaud's symptoms and the organic vascular changes have a common etiology? The results of this study indicate they have a common etiology.

*D The treatment of Raynaud's syndrome.* The treatment of Raynaud's syndrome varies with



circumstances as determined from each individual case but may follow certain broad principles, as follows:

1. No treatment necessary. In a group of patients (3 in this series) no definite etiology can be found, the symptoms are mild, and the Raynaud's syndrome shows no evidence of progression even after many years. Patient S. T. of this series illustrates this very well. She has been under observation for Raynaud's symptoms for 10 years. There has been no progress, the symptoms are very mild, and she has learned to avoid the attacks. In the meantime she has developed a cancer of the breast which is more distressing than the Raynaud's disease.

2. The treatment of associated diseases. It is very important to treat associated conditions or diseases, particularly secondary anemia and syphilis. The secondary anemia obviously involves the treatment of the cause of the anemia if it can be found.

3. Local treatment. This involves instructions to the patient to avoid the thing that brings on the attacks. Paraffin baths give considerable relief to some patients.

4. Surgery of the sympathetic nervous system. In 5 patients in the series, various types of surgery to the sympathetic nervous system were performed. No improvement was noted as judged over a period of years. Some reasons for this are in the next heading.

*E. Notes with early and late vascular effects of surgery to the sympathetic nervous system.* These effects vary with the type of operation done as follows:

1. The effects of resection of the stellate and second or third dorsal sympathetic ganglia. Immediately following this type of operation there are present, (a) an increased skin temperature of the upper extremity, (b) cessation of sweating to the upper extremity, (c) an increased circulation in the fingers, and (d) a Horner's syndrome. Heat

dilatation in the course of the median nerve by nerve block at the wrist.

2. Following the so called "preganglionic" sympathectomy to the upper extremity as done by White (1) the circulatory effects as well as any effects on heat regulation were transitory. It is doubtful that they lasted longer than the traumatic effects of the operation. Vasodilatation in the fingers could be produced following recovery from the surgery by local heat or median nerve block indicating the presence of nerves with vasomotor function.

It is difficult to reconcile many of the views expressed with some of those of the literature, especially those concerning treatment. One can say definitely that in this series of patients, medical management offered far more to the patient in the way of objective and subjective relief than surgery.

*The importance cannot be overlooked of the recognition of patients with Raynaud's symptoms as part of some other disease as compared with the recognition of Raynaud's disease (which may not even exist as a clinical entity).*

If Raynaud's disease exists as a clinical entity it must be very rare. It is doubtful if any of the patients reported in this series had the disease. If this is true the author never has seen a patient with unquestioned Raynaud's disease.

On the other hand 2 patients are reported with Raynaud's symptoms as part of some more fundamental disease. Medical management gave great deal of relief to a number of these patients. It would seem logical to conclude that it would be better to direct our attention to the recognition and treatment of Raynaud's symptoms as part of some other disease than to Raynaud's disease per se, which must be extremely

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3 In this series of patients, surgery of the sympathetic nervous system was a therapeutic failure but medical management gave considerable relief in a number of patients

## BIBLIOGRAPHY

- 1 ALLEN, E V, and BROWN, G E Raynaud's disease, a critical review of minimal requisites for diagnosis Am J M Sc, 1932, 183 187-200
- 2 HUNT, JOHN H The Raynaud phenomena, a critical review Quart J Med N S, 1936, 5 339-444
- 3 JOHNSON, CARL A The effect of amyl nitrite upon the finger volume J Lab & Clin Med, 1931, 17 59
- 4 Idem The digital plethysmograph as a measure of the peripheral circulation Surg, Gynec & Obst, 1940, 70 31-41
- 5 JOHNSON, CARL A, SCUPHAM, GEORGE W, and GILBERT, N C Studies on peripheral vascular phenomena II Observations on peripheral circulatory changes after unilateral cervical ganglionectomy and ramisectiony Surg, Gynec & Obst, 1932, 55 737
- 6 LEWIS, THOMAS Experiments relating to the peripheral mechanism involved in spasmodic arrest of the circulation in the fingers, a variety of Raynaud's disease Heart, 1929, 15 9
- 7 RAYNAUD, MAURICE L'asphyxie locale et la gangrène symétrique des extrémités Thèse de doct, 1862
- 8 Idem Nouvelles recherches sur la nature et le traitement de l'asphyxie locale des extrémités Arch gén de méd, 1874, 5 189
- 9 SMITHWICK, REGINALD H Modified dorsal sympathectomy for vascular spasm (Raynaud's disease) of the upper extremity Ann Surg, 1936, 10 339

## MUCINOUS CARCINOMA OF THE BREAST

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IT is often amazing to observe within an outspoken malignant epithelial tumor glandular or cystic structures filled with a basophilic homogeneous material in which perhaps only a few groups of carcinoma cells are still recognizable. From adjacent structures having adenocarcinomatous portions one gains the impression that perhaps this evidently secreted material has led to an atrophy and the eventual destruction of the tumor cells. In other words, the mucin which originally had been secreted by the tumor cells had subsequently caused their disappearance. Apparently because of the intriguing assumption of a seeming self-destruction of cancer cells, this type of carcinoma was early recognized as a separate variety of carcinoma, especially in the breast. As early as 1853 investigators classified this cancer of the breast as an especially benign form principally because of the conception of the destruction of the tumor cells by their own secretions.

Though this carcinoma early was recognized as a special type until recently relatively few studies have been undertaken of mucinous carcinoma of the breast. The more recent interest in this entity may perhaps be traced to the studies of Cheate and Cutler who showed that mucinous degeneration in breast carcinomas is more common than is generally supposed and emphasized that the presence of gelatinous degeneration in these tumors does not necessarily imply a low degree of malignancy as was generally supposed.

The nomenclature of these tumors is confusing. The terms colloid, gelatinous, mucoid, mucinous, and myxomatous are used indiscriminately. It seems that since mucin is the product of epithelial cells the only correct term to designate these tumors is mucinous, because these tumors are epithelial in nature and evidence of secretion is often noticeable in the individual tumor cells. Kanner emphasized the correctness of the term mucinous carcinoma. Furthermore, the staining reaction is more characteristic of mucin. According to Kanner the term colloid is used because of the brown color and gelatinous consistency. Colloid should be reserved for tumors of the thyroid gland and hypophysis which secrete

colloid. Mucoid, meaning resembling mucin, does not occur in epithelial tumors but is seen particularly commonly in connective tissue tumors. Gelatinous is purely a descriptive term referring to the similarity of the material to gelatin, but does not denote a specific substance. Yet Ewing, contrary to this, stated that true mucin is found chiefly in connective tissue tumors, pseudomucin in epithelial growth. From the foregoing it is clear that the more correct term for these tumors is mucinous carcinoma, which nomenclature will be strictly adhered to.

An opportunity presented itself to study several instances of mucinous carcinoma. Surgical specimens and autopsy material from patients who had died from this carcinoma were available. Particularly because of the latter and because it was soon realized that what was thought to constitute one group of tumors in reality consisted of several types of carcinomas, it was thought of interest to report the results of this study.

A complete review of this subject does not seem necessary. Geschickter recently reviewed in detail the available data. It may be of interest, however, to mention that as early as 1853 and 1853 Lebert, Larrey, and Robinson had studied mucinous carcinomas and stressed the slow growth of these cancers. Later curiously enough, the interest in these tumors culminated in the purely theoretical question as to whether the mucinous, or as it was called—colloid material, took its origin from the epithelial cells or from the connective tissue framework. Even among the earlier investigators there were a few who doubted the entirely benign course of these breast carcinomas. Gaube, 1908, remarked that occasionally the mucinous carcinoma may lose its mucinous characteristics, its cells may take on a high degree of anaplasia and the tumor may revert to a carcinoma of the usual type. But Shepherd, 1938 still emphasized that gelatinous carcinoma of the breast is of low malignancy and is easily cured by radical excision but if recurrence takes place, the prognosis is bad because of the insistence of the growth.

Cheate and Cutler 1931 reported 10 instances of mucinous carcinoma of the breast. They remarked upon the prevailing opinion that this is the least malignant form of a mammary carcinoma, that metastases occur late, and that the

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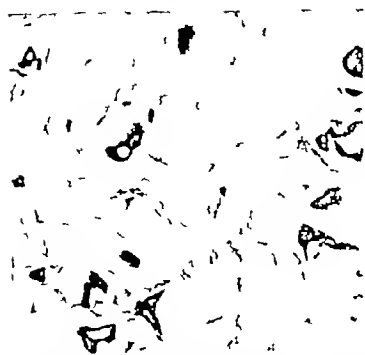


Fig 1 True mucinous carcinoma. Note the islands of tumor cells. (There are no other types of tumorous structures.) Iron hematoxylin-eosin preparation  $\times 37$ .

prognosis is more favorable. They specifically mentioned that with few exceptions the conception that this form of cancer may be highly malignant is not encountered in the literature. Five of their 10 tumors were among the most malignant, they stated, that can be encountered in the breast. Morphologically they were highly anaplastic and clinically their high degree of malignancy was demonstrated by prompt recurrence, widespread metastases, and rapid course. Lee, Hauser, and Pack, 1934, stressed the rarity of mucinous carcinoma of the breast. These investigators classified this carcinoma into (a) primary mucinous carcinoma in which the mucinous features predominate, (b) ordinary carcinoma with secondary mucinous degeneration. In these latter instances the mucinous degeneration may be recognized histologically only, whereas other portions may be highly malignant. The latter group again is subdivided into "myxoid carcinoma" in which the mucinous changes arise by metaplasia in the connective tissue whereby the latter becomes "myxomatous," and into "mucoid carcinoma,"

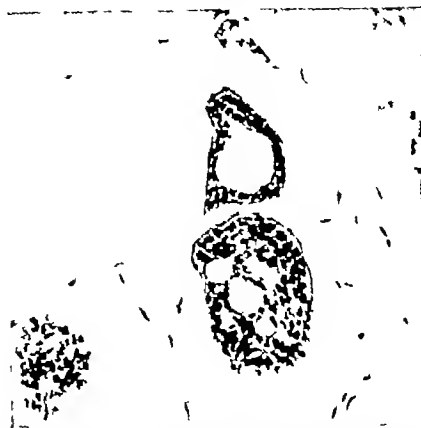


Fig 2 True mucinous carcinoma. Note the islands of tumor cells not exhibiting evidence of anaplasia, or mitotic figures. Iron hematoxylin preparation  $\times 155$ .

a variety in which the mucinous material originates directly from the carcinoma cells. It must be mentioned that this classification is made on presumptive evidence, since the authors did not offer evidence for the dual origin of the mucinous material. However, they refer to the observation of Ewing who described compact alveoli lying in broad areas of a mucous stroma with no evidence of mucous degeneration of the epithelium, as supporting the connective tissue origin of the mucinous changes. These authors also mentioned a mucinous type of tumor which has the structure of a papillary carcinoma.

Geschickter, 1938, classified these mammary cancers into two groups. In one, the tumors con-



Fig 3 Mucinous carcinomatous features in duct carcinoma. Note the duct carcinoma in the right part of the picture. Iron hematoxylin preparation  $\times 51$ .



Fig 4 Mucinous carcinomatous features in duct carcinoma. Other parts of this tumor show typical duct carcinoma. Note the islands of tumor cells and the absence of signet ring cells. Iron hematoxylin preparation  $\times 135$ .



Fig. 5. Signet ring cell mucinous carcinoma. Note the abundance of typical signet ring tumor cells. Iron hematoxylin preparation  $\times 42$ .

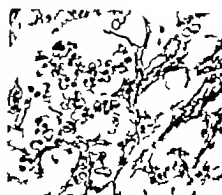


Fig. 6. Signet ring cell mucinous carcinoma. Note the signet ring cells. Fibrovascular structures. Iron hematoxylin preparation  $\times 145$ .

tain a shiny translucent gel throughout their substance and in the second group the gelatinous change is found in one or more portions, and solid, dense tissue in the remainder of the growth. It seems that Geschickter's classification is almost identical with that of Cheute and Cutler and also with that of Lee, Hauser and Pack. Among those cancers in which the mucinous changes predominate Geschickter however further mentioned a type which contains epithelium of the basal cell variety. Judging from the relatively benign character of the epithelium and from the large amount of mucinous substance he believed that the prognosis is unusually good.

Gillespie and Schmieser 1939, also stressed the rarity of these tumors. They described 3 instances of mucinous carcinoma of the breast in

which the mucinous changes were part of a medullary and of a duct carcinoma, respectively. They stressed the presence of mucinous material in adenocarcinomas of the breast, in intracystic papillary carcinoma duct, and scirrhous carcinomas.

Ewing 1941 stated that, as a rule when mucous degeneration overtakes a tumor while a rapid increase in size may follow the tumor has reached the acme of its cellular activity and its malignancy is reduced. He stressed that mucoid carcinoma is a relatively benign form of cancer.

It may be mentioned in this connection that there has also been observed in our laboratory a number of carcinomas of the breast in which the connective tissue stroma was spread by an edema-like material, sometimes resembling mu-



Fig. 7. Signet ring cell mucinous carcinoma. Note predominance of signet ring cells and also anaplastic tumor cells of duct carcinoma. Iron hematoxylin preparation  $\times 5$ .

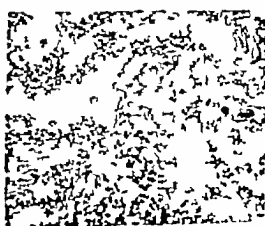


Fig. 8. Photomicrograph showing metastasis in lung of primary signet ring cell mucinous carcinoma. Iron hematoxylin preparation  $\times$ .

can These changes obviously involving the connective tissue stroma, not related to the carcinoma, do not form part of this study These are merely mentioned here because of Ewing's statement that there are evidently two types of gelatinous carcinoma, one in which the mucinous changes have involved and partly originated in the fat tissue and stroma, and one in which the alveoli are filled with mucus

This study is based on the postmortem examination of 2 patients who had died from widespread mucinous carcinoma of the breast, and on the examination of 7 breasts which had been removed for cancer which on histological examination also proved to be mucinous in character In some instances sections of the whole breast or large portions of the breast were cut according to Cheate's method In other instances serial sections of the tumors and surrounding structures were made The sections were stained with Delafield's hematoxylin and eosin or with Weigert's iron hematoxylin Elastic stains (orcein) and the van Gieson stain were employed when deemed necessary Also the mucicarmine stain for the presence of mucin was used

It is not intended to give detailed clinical histories, and only essentials which seem important will be mentioned in connection with the pathological lesions encountered

After all tumors had been examined, it seemed clear that the term "mucinous carcinoma" was rather broad and that undoubtedly various types of so called mucinous carcinoma existed These tumors have been grouped and will be discussed accordingly

*True mucinous carcinoma* Of this type only one instance was observed<sup>1</sup> Here large mucinous areas which apparently formed the bulk of the tumor were encountered The outstanding gross changes were large, circumscribed, pale yellow areas which were of semifluctuant consistency and which were separated from one another by thin strands of fibrous tissue Histologically most of the fields consisted of a pale bluish staining material often encased by a thin membrane, apparently the wall of a cyst Hardly any cellular elements were seen and only occasionally epithelial cells with vesicular nuclei and basophilic cytoplasm were encountered, singly or clustered in small groups without any particular arrangement As Lee, Hauser, and Pack expressed it, the cells were often "isolated in a sea of mucus" These cells showed no evidence of anaplasia and mitotic figures were rarely encountered The lymph nodes were not involved The patient was about

50 years of age A radical breast resection was performed and the patient is in perfect health 7 years after the operation

This tumor corresponds in every detail to the original description of mucinous carcinoma, and there seems to be no need of a more detailed description This is the type which led to the conception of the benignity of these tumors It very likely is an adenocarcinoma arising from the acini of the breast The outstanding histological findings are the presence of the mucinous material with very few cellular elements and the absence of other malignant epithelial structures

*Mucinous carcinomatous features in duct carcinoma* This is perhaps the most common type of so called mucinous carcinoma and most of the reported tumors fall into this group At least 7 of the 10 tumors reported by Cheate and Cutler come under this classification Of the 7 tumors removed surgically in this series, 5 must be designated as duct carcinoma with mucinous features

Grossly these tumors may or may not be characteristic of mucinous carcinomas, though 4 of these 5 showed large, yellowish, semifluctuant regions similar to those seen in true mucinous carcinomas But often, adjacent to these regions or sometimes in the middle of obviously mucinous areas, were firmer, grayish-pink, seemingly well circumscribed portions of tumor revealing bright yellow streaks The extent of these two portions of which the tumor consisted varied considerably The histological sections showed a mixture of typical duct carcinomatous structures and mucinous carcinoma Large tumor cells with varying amounts of cytoplasm often filled small or larger ducts Atypical mitotic figures were common and anaplasia was marked Often groups of these cells were observed, more or less isolated and infiltrating the surrounding breast structures In addition many cysts and dilated ducts were encountered, filled with a lightly stained basophilic material in which were groups of cells or isolated cells These cells showed characteristics similar to those just described Often, however, the nuclei were absent and mitotic figures were rarely encountered Often within the cyst and within the mucinous material there were outlines of, or even well preserved, minute vessels and capillaries, though the tumor cells which must have been there before could not be made out Sometimes the walls of these minute vessels were broken and many red blood corpuscles were seen within the cysts It is of interest that in one of these tumors an intracystic papilloma and in another an intracystic papillary carcinoma were also present It should be stressed here that the latter is met with not

<sup>1</sup>I am indebted to Dr Paul Klemperer for this tumor



Fig. 5. Signet ring cell mucinous carcinoma. Note the abundance of typical signet ring tumor cells. Iron hematoxylin preparation.  $\times 42$

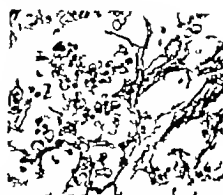


Fig. 6. Signet ring cell mucinous carcinoma. Note the signet ring cells with alveolar structures. Iron hematoxylin preparation.  $\times 145$

tain a shiny, translucent gel throughout their substance and in the second group the gelatinous change is found in one or more portions, and solid dense tissue in the remainder of the growth. It seems that Geschickter's classification is almost identical with that of Cheate and Cutler and also with that of Lee, Hauser and Pack. Among those cancers in which the mucinous changes predominate Geschickter however further mentioned a type which contains epithelium of the basal cell variety. Judging from the relatively benign character of the epithelium and from the large amount of mucinous substance, he believed that the prognosis is unusually good.

Gillespie and Schmetzer 1939 also stressed the rarity of these tumors. They described 3 instances of mucinous carcinoma of the breast in

which the mucinous changes were part of a medullary and of a duct carcinoma, respectively. They stressed the presence of mucinous material in adenocarcinomas of the breast, in intracystic papillary carcinoma, duct, and scirrhous carcinomas.

Ewing, 1940 stated that as a rule when mucous degeneration overtakes a tumor while a rapid increase in size may follow the tumor has reached the acme of its cellular activity and its malignancy is reduced. He stressed that mixed carcinoma is a relatively benign form of cancer.

It may be mentioned in this connection that there have also been observed in our laboratory a number of carcinomas of the breast in which the connective tissue stroma was spread by an edema-like material sometimes resembling mucus.

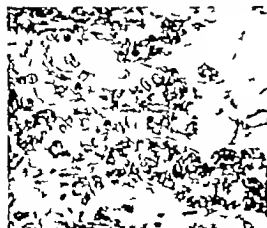


Fig. 7. Signet ring cell mucinous carcinoma. Not predominance of signet ring cells and also anaplastic tumor cells of duct carcinoma. Iron hematoxylin preparation.  $\times 5$

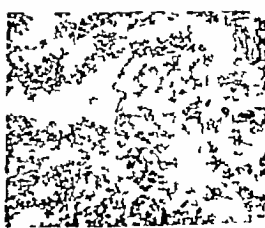


Fig. 8. Photomicrograph showing metastasis to bone of primary signet ring cell mucinous carcinoma. Iron hematoxylin preparation.  $\times 2$

velvety, broadly attached tumor which consisted of a large number of well circumscribed, small or minute excrescences. These were covered and separated from one another by mucinous material. Histologically the tumor consisted of round, oval and, more often, spindle shaped epithelial cells resembling transitional cells of the urinary tract, and an insignificant, thin, connective tissue stalk. These cells were covered by a mucinous material and much of this was also present between groups of these cells. The wall of the cyst was well preserved. Because of the spindle shaped cells the tumor could be classified as a transitional type of intracystic papilloma (Saphir and Parker). Geschickter apparently drew attention to this type of tumor, to which he referred as gelatinous carcinoma containing epithelium of the basal cell type. He stated that judging from the relatively benign character of the epithelium and from the large amount of mucoid substance, the prognosis in these growths should be unusually good.

#### EVALUATION

It has been shown that the tumors classed as mucinous carcinoma of the breast are not one entity but apparently consist of various forms of tumors of the breast, four of which have been described. The true mucinous carcinoma, originally described as colloid or gelatiniform carcinoma is said to be of low grade malignancy. Only if sections through the whole breast or serial sections show no other types of malignant structures, may such a tumor be designated as true mucinous carcinoma. This form, however, seems the rarest. Not a single such instance was observed in this laboratory among over 700 cancers of the breast, the tumor described here having been received from another laboratory. Because of the insufficient material little can be said as to the origin of this type of cancer. It is probable that this tumor arises from the acini. This is apparent because of the histological finding of many small acini and the absence of duct structures which are so common in other forms of mucinous carcinoma of the breast. It is interesting to note that Geschickter described three tumors which microscopically are indistinguishable from basal cell cancer of the adenocystic type, such as is found in the parotid gland. A portion of the growth actually may resemble benign mixed tumors of the parotid gland. He believed that typical mucoid cancer of the mammary gland may originate as a form of adenocystic basal cell cancer. It seems quite possible that these tumors may be very early forms of true mucinous carcinomas of the breast. Perhaps the adenocystic structures described by Geschick-

ter may constitute acini of the breast filled with mucin. The similarity of these early tumors to the adenocystic basal cell carcinoma is interesting because of the comparative benignity of these tumors and of the true mucinous carcinomas of the breast.

As mentioned before, the duct carcinoma of the breast with mucinous features is undoubtedly the most frequently encountered type of so called mucinous carcinoma. It seems that the mucinous changes are purely secondary, the underlying tumor being a duct carcinoma. In contradistinction to the third form, this variety shows the secreted mucin outside the tumor cells. The tumor cells are apparently soon destroyed and signet cells are not found. It is obvious that the degree of malignancy does not depend upon the presence or the amount of mucin but upon the unchanged duct carcinomatous structures.

Intracystic papilloma or intracystic papillary carcinoma are often found in these tumors, not only in this series but often in the tumors described in the literature. Though this finding offers some interesting speculation in regard to a possible relation of duct carcinoma and mucinous changes, to intracystic papilloma, this and other studies have not disclosed any relationship. It seems most likely that the simultaneous occurrence of these lesions is purely coincidental.

The signet ring cell variety is perhaps the most interesting and the two autopsy findings recall Cheate and Cutler's statement that some of the mucinous carcinomas are among the most malignant tumors encountered in the breast. The widespread metastases in both autopsied cases, the rapid recurrence in the first, and the fact that when the second patient was seen, operation was too late because of the widespread metastases, indicates the high malignancy of these tumors. In both patients the ovaries were involved and studded with signet shaped tumor cells. It must be emphasized, of course, that in neither of the patients was a primary malignant tumor encountered in the gastro-intestinal tract, though metastatic tumors were found in the wall of the small intestine in the second patient. This suggests, perhaps, a peculiar affinity of these signet shaped tumor cells for the ovaries as seen in carcinoma of the stomach with signet ring cells—metastases to the ovaries (Krukenberg's tumor). On the other hand, however, it is interesting to note that one patient whose breast was radically removed for eradication of such a tumor is apparently well, four years postoperatively.

This variety of mucinous carcinoma is also found in combinations with duct carcinoma



rarely in outspoken duct carcinomas. The former probably is a coincidental finding and might not have been discovered had not the entire breast been examined.

As mentioned previously "mucinous features" in duct carcinomas constitute the most common form of so called mucinous carcinoma. In these tumors the presence of mucin is apparently incidental and the tumor follows, as a rule, the course of a duct carcinoma. These tumors apparently belong to those mucinous carcinomas concerning which Ewing remarked that they may prove highly malignant. This he explained by the distention of tissue spaces by the mucus which distention supposedly facilitates the dissemination of the surviving cells.

**Signet ring cell mucinous carcinoma.** This type of carcinoma consists predominantly of secreting tumor cells. So much secretion is retained within the cells that they assume signet ring shapes. Three such tumors were encountered. One of these was a surgical specimen and the 2 others were found at postmortem examination. The surgically removed tumor was found beneath the nipple and consisted of a rather firm, ill defined mass measuring 4 centimeters in greatest dimension. The nipple was not fixed. On section the tumor was grayish-white but showed a few yellowish glistening and bulging areas. In the remainder of the breast foci of fibrosis and cysts were recognized. With the exception of these glistening areas there was nothing noted from which the mucinous character of the tumor might have been inferred. Histologically the tumor consisted mainly of well circumscribed foci of epithelial cells which showed either a lightly stained basophilic cytoplasm with nuclei situated at the base of the cells which often assumed the typical signet ring forms. Often the cytoplasm in the sections seemed clear, only the cell membranes and the crescent shaped nuclei being recognizable. In other fields small or larger cystic structures could be noted filled with a basophilic material and relatively few epithelial cells. However instead of clumps of epithelial cells with clear cut, round nuclei and basophilic cytoplasm as seen in the true mucinous carcinomas, the cells suspended in the cystic structures here were signet shaped and had clear cytoplasm. These cells were also often seen isolated from ducts or acini, invading the stroma. Serial sections of the breast, however, also showed ducts which were crowded with tumor cells which either were typical of duct carcinoma cells with many anaplastic cells and numerous atypical mitotic figures or showed transition to signet ring cells as described. Some fields showed duct carci-

nomatous structures and adjoining these accumulations of signet ring cells. Metastases to the axillary lymph nodes consisted only of the signet shaped tumor cells. The patient, a 53 year old white female, had noted the tumor only a short time before consulting the physician. A radical mastectomy was performed, not followed by radiation treatment and the patient, after 4 years, is apparently well.

A similar tumor was found in the 2 patients who came to autopsy. In the first instance, a 35 year old white female, a radical breast amputation had been performed 4 months before death. The autopsy revealed a local recurrence and metastases to the sternum, mediastinal lymph nodes, peritoneum, inguinal lymph nodes, liver and both ovaries. As a matter of fact, both ovaries were so markedly enlarged—measuring about 12 centimeters in greatest dimension—that at first they were thought to be the seat of primary solid tumors. The tumors histologically consisted principally of slightly basophilic cells with flattened, crescent shaped nuclei. When the previously removed breast tumor was examined, sometime later it proved to be histologically a duct carcinoma with transitions to the mucus secreting signet shaped cells just described. In the second autopsy the tumor was found in the left breast of a 49 year old colored female. It measured 4 by 5 by 5 centimeters in greatest dimensions, was of a rather firm consistency but was not noticed by the patient until shortly before she entered the hospital, where she died before treatment could be instituted. The autopsy revealed metastases in the axillary lymph nodes, pleura, lungs, pericardium, peritoneum, intestinal wall, retroperitoneal lymph nodes, suprarenal glands, ovaries, and spinal column. Histologically the breast tumor consisted mainly of signet ring cells either arranged in groups or singly invading the surrounding stroma. However serial sections also revealed outspoken duct carcinomatous structures. The metastases, however, consisted only of the signet ring cells.

**Intracystic papilloma with mucinous features.** Only one such tumor was observed. This was found in a 47 year old woman who had a small tumor in the left breast which suddenly became enlarged, at which time a hemorrhagic discharge from the nipple was noted. Grossly the tumor consisted of a cyst measuring about 4 centimeters in greatest dimension, which was filled with a hemorrhagic and mucinous material in which small, yellowish pieces of soft, granular tissue were found loosely intermingled. The inner wall of the cyst presented a rather soft and friable,

velvety, broadly attached tumor which consisted of a large number of well circumscribed, small or minute excrescences. These were covered and separated from one another by mucinous material. Histologically the tumor consisted of round, oval and, more often, spindle shaped epithelial cells resembling transitional cells of the urinary tract, and an insignificant, thin, connective tissue stalk. These cells were covered by a mucinous material and much of this was also present between groups of these cells. The wall of the cyst was well preserved. Because of the spindle shaped cells the tumor could be classified as a transitional type of intracystic papilloma (Saphir and Parker). Geschickter apparently drew attention to this type of tumor, to which he referred as gelatinous carcinoma containing epithelium of the basal cell type. He stated that judging from the relatively benign character of the epithelium and from the large amount of mucoid substance, the prognosis in these growths should be unusually good.

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This variety of mucinous carcinoma is also found in combinations with duct carcinoma.

However whereas in the signet cell variety the individual secreting tumor cells remain intact, but lose their connections with the duct structures, invade diffusely the surrounding breast and produce widespread metastases, in the second variety here described, the secreting tumor cells are apparently destroyed and only the duct carcinoma cells are responsible for the behavior of the tumor. It may be mentioned in this connection that Gillespie and Schmeissner described in one of their three tumors scattered epithelial elements separated by a loose stroma filled with mucin. There were solid nests of cells or definite gland formations. Some of the cells contained transparent droplets. Others were distended with mucinous material which pushed the nuclei aside, causing a signet ring appearance.

The intracystic papilloma with mucinous features is apparently not a malignant tumor but probably behaves as the transitional cell papilloma (Saphir and Parker). The benignity of these tumors was indicated by Geschickter who stated that 19 of his 25 patients showing this tumor were traced. With the exception of 3 dying from other causes, all survived the 5 year period.

#### SUMMARY

This study reveals that mucinous carcinoma of the breast is not a single entity but can be classified into at least four definite types of tumors. The *true mucinous carcinoma* consists of duct or cystic structures filled with mucinous material in which groups of or isolated, tumor cells may still be recognizable here and there. There are no other tumor structures present. This is apparently a rare tumor which clinically is relatively benign. The original conception of the benignity of these tumors must be traced to this variety of mucinous carcinoma of the breast. The *duct carcinoma with mucinous features* is the most common type. Areas similar to those seen in true mucinous carcinoma are intermingled with duct carcinomatous structures. Sometimes, however, these latter portions are seen only after sections of the whole breast have been examined. These tumors are just as malignant as simple duct car-

cinomas. The *signet ring cell mucinous carcinoma* is characterized histologically by well preserved mucin secreting cells with basophilic or clear cytoplasm and crescent shaped, compressed nuclei situated at the base of the cells. Whereas in the two former groups the secreting cells are soon destroyed, disappear and large spaces filled with mucin remain, in the third group the signet ring tumor cells remain intact. Soon they become isolated from ducts and acini, invade the stroma and may produce the most widespread metastases, particularly in the ovaries. Though duct carcinomatous structures may also be present in this variety the metastases consist mostly of signet ring shaped cancer cells. This tumor is regarded as highly malignant. Two patients died from widespread metastases soon after the detection of the primary tumor. Yet one patient is alive 4 years after operation. The fourth variety may be designated as *intracystic papilloma with mucinous features*. This is a relatively rare, nonmalignant tumor.

#### BIBLIOGRAPHY

- CHESLEY, G. L., and CUTLER, M. Tumors of the Breast. Philadelphia and Montreal: J. B. Lippincott Co. 93.
- E. H. J. Neoplastic Diseases, 4th ed. Philadelphia and London: W. B. Saunders & Co., 940.
- GAARE, G. Die Gallertkrebs der Brustdrüse. Beitr. Klin. Chir., 90, 60-760.
- GESCHICKTER, C. F. Gelatinous mammary cancer. Ann. Surg., 93, 283-2.
- GILLESPIE, C. E., and SCHMEISSNER, H. C. Mucoid carcinoma of the breast. South. M. J. 1930, 33: 629.
- KARNER, H. T. Human Pathology 4th ed. Philadelphia and London: J. B. Lippincott Co., 921.
- LARRET, M. Tumeur gélatineuse ou colloïde de la mammaie. Bull. Soc. de chir. de Paris, 1853, 3: 545.
- LEBERT, H. Befunde zur Kenntnis des Gallertkrebses. Arch. f. path. Anat. et 85, 4: 92.
- LEE, B. J. HATCHER, H., and PAGE, G. T. Gelatinous carcinoma of the breast. Surg. Gynec. & Obst. 93, 50-54.
- ROBINSON, R. B. Gelatinous cancer of the breast. T. Path. Soc. Lond., 85, 4: 775.
- SAPHIR, O. and PARKER, M. L. Intracystic papilloma of the breast. Am. J. Path. 940, 6: 89.
- SCHMEISSNER, W. F. Carcinoma of the breast. Arch. Surg. 93, 57-90.

# THE ACCURACY OF ROENTGEN ESTIMATES OF PELVIC AND FETAL DIAMETERS

A LOUIS DIPPEL, M D , F A C S , and E DELFS, M D , Baltimore, Maryland

MODERN roentgen pelvimetry and fetometry have been extensively developed during the past 6 years. As a result, they have been utilized by many hospitals and teaching institutions, in some, routinely in every primigravida and in every multipara with a previous history of difficult labor or delivery, and in others, only in selected cases, such cases being chosen for roentgen study after careful external and internal clinical mensuration and palpation. There are still, however, many obstetricians who do not utilize this valuable clinical aid. In some localities the number of definitely contracted pelvis is relatively so small that roentgen pelvimetry is not often necessary and, under these circumstances, no urgent need is felt for the information obtained from roentgen pelvimetry and fetometry. Furthermore, there are many obstetricians who have not been convinced of the precision of these roentgen procedures. It cannot be said that these clinicians refuse to be convinced, but rather that those of us working in the field of obstetrical roentgenography have not placed sufficient importance upon the precision of our various techniques and have not emphasized the range of probable error in each. The main purpose of this paper is to attempt to evaluate the precision of several commonly employed roentgen methods of pelvimetry and fetometry.

The simplest technique, and the one most universally utilized in this country today, is the position method devised and perfected by Thoms (18-21), and modified by Torpin. Walton's method may be included here, since it depends upon essentially the same principles. The accuracy of the pelvic estimations from the inlet view, by these methods, is dependent solely upon the ability of the clinician or the x-ray technician to locate the plane of the pelvic inlet from external bony landmarks. As early as 1789, Baudelocque contended that the plane of the inlet lay in the plane located by the upper border of the symphysis pubis, anteriorly, and the depression beneath the spine of the fifth lumbar vertebra, posteriorly. It soon became evident to both anatomists and

obstetricians that this was rarely the case, and roentgenologists have repeatedly shown that the posterior external landmark lies at a much lower level than the sacral promontory or even the projection of the iliopectineal lines on the sacrum. Accordingly, Thoms (21) has elevated the posterior external landmark until at present his technician marks the depression beneath the spine of the third lumbar vertebra. Torpin uses as the posterior endpoint the space lying between the spinous processes of the fourth and the fifth lumbar vertebrae.

It must not be forgotten that there is considerable individual variation in pelvis and that often the plane of the pelvic inlet will not be located precisely from even these currently employed bony landmarks. However, Thoms (21) says that his "experiments with dried pelvises have shown us that this posterior point may vary as much as 2.5 centimeters above or below the ideal situation, without measurably affecting the mensuration as recorded on the film." Since he measures to the nearest one-quarter of a centimeter on the film, it follows that his maximum error should be  $\pm 2.5$  millimeters, provided the anterior external landmark is correctly located and the posterior one is selected not more than 2.5 centimeters above or below the ideal location. The error under these circumstances can be mathematically proved to be not in excess of  $\pm 2.1$  per cent. The only means of determining the correctness by which these external landmarks are located is to observe the selected ones on the lateral film. Thoms (21) suggests that this lateral film could be taken first and developed before selecting the ideal location for the posterior external landmark. This should remove all doubt concerning the precision of the estimates made of the pelvis from its inlet view. Our own experience with the use of lead shot over the external landmarks, in 25 cases, has shown that such a step is necessary if the plane of the pelvic inlet is to be closely enough approximated by the plane of the external landmarks to keep the error consistently below 5 per cent. However, apparently without this precautionary step, Schumann measured the anteroposterior and transverse diameters of the pelvic inlet in a group of women,

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tance of the object below the x-ray tube (166.88 cm)

From similar triangles

$$\frac{AB}{10} = \frac{a}{166.88} = \frac{TH}{182.88}$$

or,  $10 \times 166.88 = ab = 182.88$

solving,  $166.88 \times ab = 182.88$

$$ab = 10.96 \text{ cm}$$

But, 10 cm = 100% of actual length of the object,

and, 10.96 cm = 109.6% of actual length of the object,

or 0.96 cm. = 9.6% of actual length of the object

Therefore, 9.6 per cent represents the amount of triangular distortion of a pelvic diameter in a lateral teleroortgenogram. Thus it is seen that pelvic or fetal estimates from teleroortgenograms are overestimated by essentially 10 per cent under normal pelvic conditions. Any haphazard position method, or even a rough guess at the object-film distance, would produce more accurate results. Moreover, much bony detail is sacrificed in reducing the amount of triangular distortion by increasing the tube-film distance.

All stereoscopic methods may be considered together, for they differ only in the instruments employed in working up the material. These methods have the advantage over the position methods that they require no positioning of the patient other than to show the pelvic diameters to best advantage, and their accuracy is not based upon the correct localization of external bony landmarks, nevertheless there are steps in procuring these roentgenograms which require precision. For instance, it is necessary to employ register or centering markers, so that when these, in each pair of stereoscopic films, are accurately superimposed, the result obtained is exactly the same as though both exposures had been made on a single negative. This can be accomplished with relative ease by adding permanent or removable markers to the cassette carrier. Another equally important precaution is to employ the precise tube-film and tube-shift distances which are called for by the particular technique being used. Failure to observe the latter rule is probably the most common cause of technical errors in stereoscopic pelvimetry.

The ideal means of avoiding such errors would be the construction of a precise x-ray machine, such as the one in Hodges' (10) laboratory, for not only have the tube-film and tube-shift distances been precisely calibrated, but they can not be altered. If the technician then utilizes the total available tube-shift distances, there can be no question that these films are precise and estimations from them should be as nearly 100 per cent accurate as human error in interpreting them will allow. Unfortunately, no other x-ray laboratory

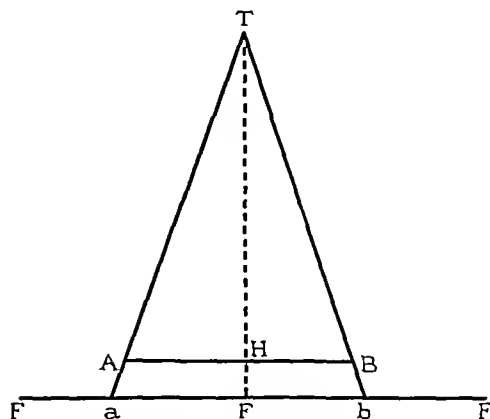


Fig. 1. Diagram indicating the distortion resulting from teleroortgenography.

has produced a similar precision x-ray machine and all other investigators have continued to utilize more or less non-precise x-ray machines. As a result, practically all these others have inserted into each pair of stereoscopic films, a radioopaque marker of known length. The position of this marker is immaterial, the only requirement being that it appear in each film and that its position remain unchanged until both of a pair of stereoscopic films have been obtained. The chief point of interest lies in the attitude of various investigators toward this known marker.

Clifford (6, 7) measures the control markers in each pair of films and says that if the method has been executed properly, the maximum error should be 0.2 centimeter, in other words, the maximum technical error should be  $\pm 2.0$  per cent, for the control markers are actually 10 centimeters long. In those instances in which the technical error is greater, it has been customary at the Boston Lying-In Hospital to repeat the procedure, or to indicate that the results are not extremely reliable. Clifford reports an accuracy of within 3 millimeters in 97 per cent of the Class A films, i.e., those in which there has been no fetal head movement between or during the stereoscopic exposures. Since the classification of his films depends upon the presence or absence of evidence of fetal head movement, the accuracy of estimates of the pelvic diameters should be equally as good as the figures given, provided the endpoints are clearly visualized, for movement of the maternal pelvis between, or during, exposures is rare.

Johnson (13, 14) inserts a marker of known length into his stereoscopic films, but apparently does not measure its images routinely with his stereoroentgenometer. Since the basic principle

both at laparotomy and from a roentgen inlet view made by Thoms technique and they came to the conclusion that the variation in length of each diameter, as determined by the two means, was constantly less than 2.0 millimeters.

The extent of error in the anteroposterior pelvic diameters, as determined from the Thoms lateral roentgenogram should amount only to that due to human error in applying a caliper length to a distorted centimeter scale, plus the probable error due to poor visualization of the endpoints of those diameters. This latter becomes a definite entity to be reckoned with when we deal with diameters extending to or from the lower margin of the symphysis pubis the same is true of the ischial tuberosities, which, even with very good roentgen technique, are often not clearly outlined on the roentgenogram. Nevertheless, with accurate placing of the lead ruler and the production of a true lateral view of the pelvis, the precision by this method should reach a very high degree of accuracy in symmetrical pelvis, for the intergluteal fold in all such cases probably lies in the sagittal plane of the pelvis. The same can be said of the lateral roentgenogram which is being developed by Hodges (12) and in which one-half the bitrochanteric diameter is used as the object-film distance.

The accuracy of roentgen cephalometry by the position methods mentioned leaves much to be desired. The precise determination of the distance between the geographical center of the fetal head, or between the endpoints of any fetal diameter and the film, is the great source of error. Walton, however has devised a unique method of checking the accuracy of his object-film distances. Lead markers are fixed to the anterior and to one lateral wall of the abdomen, over what is believed to be the geographical center of the fetal head, in each anteroposterior and lateral view. Both anteroposterior and lateral roentgenograms are taken without shifting the position of the patient from the supine. If the image of the radio-opaque marker appears at or near the geographical center of the fetal head, the previously recorded object-film distance can be used and accurate estimations of fetal head diameters anticipated.

Ball's method (-3) has gained considerable popularity during the past few years and affords the minimum of mathematical manipulation. His present cephalometer (3) consists of a nomographic chart with a movable indicating member which carries the calculations from the raw data immediately to the estimate of the length of the pelvic or fetal head diameter with one step

The estimation by the Ball method, of the object-film distance of any pelvic or fetal head diameter appearing, for instance, in the lateral view is made from bony landmarks appearing in the anteroposterior view and includes the use of certain empiricisms. Thus, the object-film distance for the obstetrical conjugate diameter is estimated by measuring, on the anteroposterior film, the distance between the symphysis pubis and a point on the greater trochanter to which must be added the table top to film distance. The point on the greater trochanter is a variable one and depends upon the tube-film distance used, being more laterally placed with greater tube-film distances. Ball believes that the distance between the point on the greater trochanter and the lateral surface of the thigh represents the amount of triangular distortion in the lateral film. He (3) has compared one-half the bitrochanteric diameter as measured upon the patient, with the diameter obtained from bony landmarks, and has found that these correspond so closely that he believes arbitrary bony landmarks sufficiently accurate for practical purposes. However in an earlier communication, he says that "the pelvic diameters are considered to be accurate to within 5 mm. The mean circumference of the fetal head is accurate to within 1 cm. In the majority of cases and 3 cm. in all cases." In a more recent article (2) he concludes that "in general it may be said that there has been a maximum error of 10 per cent in fetal head volume and 5 per cent in linear diameter measurements."

From time to time, since Vernier's work, in 1900, one investigator or another has rediscovered the idea that there is less distortion of an object when roentgenographed at a tube-film distance of 6 feet than at the more commonly employed tube-film distances, and has proposed that roentgenograms with the former technique represent undistorted radiography. Buchner has recently utilized this procedure in obstetrics, but we discuss the method only to indicate the relatively large radiographic distortion in teleroentgenograms, and to show that they are neither accurate nor record prenatal findings without bias. This can best be shown by similar triangles, as follows (Fig. 1)

Let  $FF$  represent the film,  $T$  the x-ray tube  $AB$  a pelvic diameter which for convenience we assume measures 10 centimeters and  $HF$  an object-film distance of 16 centimeters, i.e., one-half the normal bitrochanteric diameter. The  $ab$  represents the projection of  $AB$  on  $FF$  when roentgenographed from a tube-film distance,  $TF$  of 6 feet (182.88 cm.) and  $TII$  represents the dis-

tance of the object below the x-ray tube (166.88 cm)

From similar triangles

$$\frac{AB}{10} = \frac{a}{166.88} = \frac{b}{182.88}$$

or,  $10 \cdot a = 166.88 \cdot b$

solving,  $166.88 \cdot ab = 182.88 \cdot 3 \text{ cm}$

$$ab = 10.96 \text{ cm}$$

But, 10 cm = 100% of actual length of the object,

and, 10.96 cm = 109.6% of actual length of the object,

or 0.96 cm = 9.6% of actual length of the object.

Therefore, 9.6 per cent represents the amount of triangular distortion of a pelvic diameter in a lateral teleroentgenogram. Thus it is seen that pelvic or fetal estimates from teleroentgenograms are overestimated by essentially 10 per cent under normal pelvic conditions. Any haphazard position method, or even a rough guess at the object-film distance, would produce more accurate results. Moreover, much bony detail is sacrificed in reducing the amount of triangular distortion by increasing the tube-film distance.

All stereoscopic methods may be considered together, for they differ only in the instruments employed in working up the material. These methods have the advantage over the position methods that they require no positioning of the patient other than to show the pelvic diameters to best advantage, and their accuracy is not based upon the correct localization of external bony landmarks, nevertheless there are steps in procuring these roentgenograms which require precision. For instance, it is necessary to employ register or centering markers, so that when these, in each pair of stereoscopic films, are accurately superimposed, the result obtained is exactly the same as though both exposures had been made on a single negative. This can be accomplished with relative ease by adding permanent or removable markers to the cassette carrier. Another equally important precaution is to employ the precise tube-film and tube-shift distances which are called for by the particular technique being used. Failure to observe the latter rule is probably the most common cause of technical errors in stereoscopic pelvimetry.

The ideal means of avoiding such errors would be the construction of a precise x-ray machine, such as the one in Hodges' (10) laboratory, for not only have the tube-film and tube-shift distances been precisely calibrated, but they can not be altered. If the technician then utilizes the total available tube-shift distances, there can be no question that these films are precise and estimations from them should be as nearly 100 per cent accurate as human error in interpreting them will allow. Unfortunately, no other x-ray laboratory

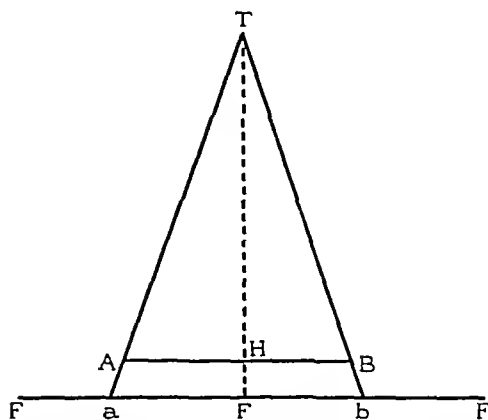


Fig. 1. Diagram indicating the distortion resulting from teleroentgenography.

has produced a similar precision x-ray machine and all other investigators have continued to utilize more or less non-precise x-ray machines. As a result, practically all these others have inserted into each pair of stereoscopic films, a radio-opaque marker of known length. The position of this marker is immaterial, the only requirement being that it appear in each film and that its position remain unchanged until both of a pair of stereoscopic films have been obtained. The chief point of interest lies in the attitude of various investigators toward this known marker.

Clifford (6, 7) measures the control markers in each pair of films and says that if the method has been executed properly, the maximum error should be 0.2 centimeter, in other words, the maximum technical error should be  $\pm 2$  per cent, for the control markers are actually 10 centimeters long. In those instances in which the technical error is greater, it has been customary at the Boston Lying-In Hospital to repeat the procedure, or to indicate that the results are not extremely reliable. Clifford reports an accuracy of within 3 millimeters in 97 per cent of the Class A films, i.e., those in which there has been no fetal head movement between or during the stereoscopic exposures. Since the classification of his films depends upon the presence or absence of evidence of fetal head movement, the accuracy of estimates of the pelvic diameters should be equally as good as the figures given, provided the endpoints are clearly visualized, for movement of the maternal pelvis between, or during, exposures is rare.

Johnson (13, 14) inserts a marker of known length into his stereoscopic films, but apparently does not measure its images routinely with his stereoroentgenometer. Since the basic principle

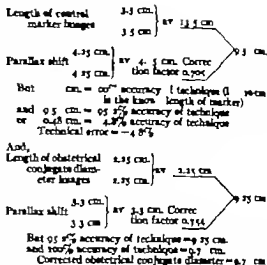


of stereorengiometry is sound, he does not consider it to be of great importance to establish the accuracy of his particular stereoscopic x ray machine.

Although Caldwell and his co-workers are primarily interested in pelvic morphology we find in the Mfology precision stereoscope (15, 16) not only a recognition of technical error but also the first utilization of it. After inserting their anteroposterior films into the precision stereoscope and before measuring the pelvic diameters with it, Mfology and Swenson (16) first measure the projected image of the known marker. If this measurement does not coincide with the known length of the marker, they alter the position of the optical system of the stereoscope and remeasure the image of the known marker. This procedure is continued until the measured length of the marker image coincides with its known length. By this procedure, the projected image of the pelvis should of necessity duplicate precisely the actual size of the pelvis. No statement on the accuracy of their estimates of pelvic diameters is made, since the accuracy is entirely dependent upon the experience of the observer with their stereoscope and upon his original stereoscopic scene.

During the development of the technique for the roentgen pelvimetry and fetometry studies at the Johns Hopkins Hospital, we realized the need of control markers of known length and some accounting of the technical errors, for the available x ray machine was not precise. In each pair

of stereoscopic films, the estimated length of the known marker was calculated by the graphic method of Hodges (10, 11). The deviation of this estimate above or below the known length of the marker was considered a positive or a negative technical error and its magnitude expressed in terms of percentage of the known length of the marker. At the same time, we were measuring the obstetrical conjugate diameter of the pelvis at the time of each laparotomy on the service. We noted, as was to be expected, that the smaller the roentgen technical error the more closely the roentgen estimate of the diameter approached its actual length, as measured at operation. We then reasoned that we had been estimating the nature and the magnitude of the technical error from the marker of known length and that we should be able to correct all our original estimates of pelvic diameters to the extent of this technical error and produce estimates of the pelvic diameters which were of essentially 100 per cent accuracy. The following was the course of procedure:



This procedure resulted in the corrected roentgen figure approaching the actual length of the pelvic diameter somewhat more closely than the uncorrected figure, but the corrected figure and the actual length of the pelvic diameter never coincided exactly. However this procedure made it possible for us to report in an earlier paper (8) an average roentgen accuracy in measuring the obstetrical conjugate diameter of  $\pm 1.6$  millimeters in 25 patients. Moreover the technical error in each of these was never in excess of  $\pm 5$  per cent. A further study of such comparative figures showed that negative technical errors resulted in overestimates of the pelvic diameters and positive technical errors in underestimates, the extent of the overestimate or underestimate depending upon the magnitude of the technical error.

The following mathematical procedures show a means of calculating the precise length of a pelvic diameter from the pair of stereoscopic films used for the mathematical calculations given, i.e., films produced by a non-precision x ray machine and showing a definite technical error.

True length known marker = its image length  $F$  (a correction factor)

Substituting available data  $10 = 3.5 F$   
and, solving,  $F = 0.74$ , i.e., this correction factor applied to the image length of the known marker will give the true length of that marker — cm.

Now  $F = \frac{K}{P + K}$  where  $K$  = tube shift distance and  $P$  = measured parallax shift

Substituting,  $74 = \frac{K}{4.25 + K}$

Solving,  $K =$  cm. 1. In obtaining the above pair of films total tube-shift of 2.1 cm. was used

instead of 10.16 cm. We assume that essentially the correct tube-film distance, 91.44 cm., was used, since it is more easily measured with precision on the x-ray machine than the tube shift distance and since errors in tube film distance do not produce as great technical errors as do errors in total tube shift distance.

Then, solving for the true length of the obstetrical conjugate

$$\text{as above, } F = \frac{K}{P + K}$$

$$\text{Substituting, } F = \frac{12.1}{3.3 + 12.1}$$

Solving,  $F = 0.786$  (correction factor for the obstetrical conjugate images obtained from the actually employed roentgen technique)

Furthermore

$$\begin{aligned} \text{True length of obstetrical conjugate} &= \text{its image length} \times F \\ &= 12.25 \times 0.786 \\ &= 9.62 \end{aligned}$$

This obstetrical conjugate actually measured 9.6 cm. at laparotomy and this estimate is much more precise than the uncorrected roentgen figure, even more precise than the corrected estimate for it

Thus, it is seen that it is possible to obtain precise estimations of pelvic diameters by this means of utilizing the marker of known length and from its images calculating the actual tube-shift distance used by a non-precision x-ray machine. The overestimate of the pelvic diameter from a use of the magnitude and nature of the technical error was not great. However, longer diameters at greater object-film distances have been found to result in errors amounting to more than 6.0 millimeters when calculated by the use of the technical error. This is true since the curve for triangular distortion correction factors is not a straight line, and this fact also explains why the use of the technical error method of correction does not result in precise estimations of pelvic or fetal diameters. If the curve were in reality a straight line, the latter procedure would be mathematically sound.

By comparing the estimate of a pelvic diameter obtained by the precision method described (i.e., by calculating from the known marker images, the actual tube-shift distance employed and then determining the correction factor for this tube-shift and the tube-film distance) with the uncorrected and corrected estimates of the same diameter as obtained by the application of the technical error, we have noted a strikingly close approximation of the average of these last two estimates to the former. These approximations are shown in the appended table. It is, therefore, shown that the shorter mathematical procedure represented by the use of the technical error method can be used and will produce re-

markably precise estimates of pelvic and fetal diameters

An immediate objection to the last described methods will be that they entail considerable mathematical manipulation. This is, of course, true, but such mathematics is usually simple arithmetic, never more complicated than high school algebra. Furthermore, if we expect to attain precision, it will probably not be accomplished through great simplicity. We do not propose that it should be necessary to go through a lengthy mathematical procedure routinely for every available pelvic or fetal diameter, in every pair of stereoscopic films. What we do wish to emphasize, however, is the need for determining the technical error in every pair of stereoscopic roentgenograms obtained by a non-precision x-ray machine and the utilization of this error, when it is a sizable one, in cases of borderline pelvic contraction. Only in such a manner will it be possible to furnish precise estimates of maternal pelvic or fetal diameters in cases in which precision will definitely indicate a choice between spontaneous delivery or a more radical elective procedure.

Recently, Friedman and Euphrat have published a preliminary report of a parallax method based upon principles originally described by Hodges and Ledoux (10). The results obtained with this method were highly accurate in measuring a dried pelvis. They have demonstrated that some mathematical manipulation may be avoided and extremely accurate pelvic estimates obtained by simply locating the footpoints of the target from its respective stereoscopic positions and utilizing these. It would seem that this should be a relatively simple and highly accurate method for diameters which are parallel to the film, provided the footpoints can be accurately located. This latter task may necessitate some calibration of the x-ray machine, if precision is to be consistently obtained. Moreover, the calculation of diameters which are not parallel to the film will require additional but simple mathematical procedure, as well as some precise knowledge of tube-film and tube-shift distances. However, this method offers valuable possibilities for the accurate determination of most of the important obstetrical diameters from stereoscopic films which are produced by the average roentgen-ray equipment.

During the past 5 years, we have primarily employed the Hodges graphic method, with the modifications described, to obtain more precise end-results than were otherwise possible with the nonprecision x-ray machine at our disposal. During the past year, we have occasionally resorted



Fig. 2. Photograph of precision caliper used in measuring pelvic diameter at the time of laparotomy. It is made of two cylinders, one telescoping into the other on screw and is calibrated in one-tenths of millimeter. The surface of one end is slightly curved, so that it will fit snugly on the sacral promontory when measuring the obstetrical conjugate. The curved plate on the outer cylinder is for purposes of grasping and holding the instrument between the fingers of one hand while the other hand is used to screw the inner cylinder in or out until the instrument fits snugly between the endpoints of the pelvic diameter.

to the precision method for the calculation of extremely important pelvic diameters in cases of cephalopelvic disproportion or markedly contracted pelvis. Also, in search of simpler yet precise technical and mathematical methods, we have tried several other methods in current use in this country. Finally a series of patients were measured by these several methods and certain actual pelvic measurements obtained with a precise caliper (Fig. 2) at laparotomy; museum specimens of bony pelvis were similarly studied. Table I shows a few comparative estimates and measurements of obstetrical conjugate diameter.

It has been our experience that the technical difficulties with measurement of pelvic diameters at laparotomy are great, in spite of the use of a precision instrument and even on a diameter with as definite endpoints as the obstetrical conjugate. In our opinion, it is for this reason that roentgen estimates of a pelvic diameter more closely approach the actual measurement on a museum specimen of a pelvis than on the living subject at laparotomy.

In Table I the Hodges graphic method indicates our own modifications of his original method. We consider the average figures from this method to be the most precise from any method we have thus far used with a nonpressure x ray machine, except possibly for the precision method. We have continued to use the former since pelvic diameters may be estimated from a previously calculated table of triangular distortion correction factors, thus eliminating the necessity for calculating the correction factor for each diameter to be estimated. Our stereorontgenometer is of the Hodges (11) type and furnishes highly accurate estimates when the technical error is small. However when these errors are large, we can not expect a high degree of accuracy for the stereorontgenometer. It is set for the roentgen technique supposed to have been employed in obtaining the stereoscopic films. Yet, as is shown in the table, the end-results are quite accurate when we utilize the technical error method of correction, as in the case of the graphic method and obtain the average between corrected and uncorrected estimates. Furthermore, as will be seen in the table, the corrected figures are over estimates to almost exactly the same degree as the uncorrected figures are underestimates, quite irrespective of the method of measurement of the nonpressure stereoscopic films. The footpoint method is essentially the same as that described by Friedman and Ephrat, except that the target footpoints were located by means of a simple device developed in Hodges' laboratory and is a method which requires no precise knowledge of the x ray factors employed in obtaining the stereoscopic films except for the tube-film distance. Further precise information is of course, necessary in this method only when the pelvic diameter to be measured lies at an angle to the film.

TABLE I—ESTIMATES OF THE LENGTH OF THE OBSTETRICAL CONJUGATE

Subject of study	Methods employed, with resultant estimates and direct measurements of obstetrical conjugate									
	Hodges graphic			Precision	Stereorontgenometer			Ferguson	Thomas indirect	Direct measurement
	Uncorrected	Corrected	Average		Uncorrected	Corrected	Average			
Pelvis A			46	45	65	19 12	96	—	—	66
Pelvis B	8	36	5	47	26	19	43	19 36	—	46
Patient L. J.	34		13 00	60	35	95	94	17 00		17.43
Patient I. R.	19	75	60 50	61	26 55		19	60 00	18 00	60.61
Patient E. M.		26 46	60 50	49	18 30	19 16	36	27	17 10	19 30
Patient T. W.	40		5	51	30	95		60	46	51

\*Obtained from several roentgen methods compared with the direct measurement obtained from two museum specimens of bony pelvis and from our patients at the time of laparotomy.

The end-results obtained by this method are generally quite accurate and with further experience, such inaccuracies as shown under patient L J, can be avoided. An error was anticipated in this case, since the footpoints fell very near to the longitudinal plane of the pelvis. As a rule, the estimates from the "Thoms lateral" view were quite accurate. Our errors with this method have undoubtedly resulted from not placing the lead ruler in the median plane of the pelvis. Such errors were usually avoided by the "Hodges lateral" method (not shown in the table), in which one-half the clinical bitrochanteric measurement is used as the object-film distance. However, it is true that both of these latter two methods will produce errors in certain asymmetrical pelvis.

Results from lateral pelvimetry alone have been recorded here, although quite similar results were obtained in these subjects from anteroposterior pelvimetry. The true endpoints of the greatest transverse diameter of the inlet are more difficult to make out, both on roentgenograms and at operation, than those of the obstetrical conjugate in the lateral view, and hence transverse measurements do not lend themselves as readily to comparisons. However, good results were obtained with the Hodges graphic, precision, and stereoroentgenometer methods, when used as for the lateral view. The accuracy of the footpoint method varied somewhat, aside from the occasional incorrect lateral placement of the target footpoints. The results with the Thoms inlet view varied directly with the precision by which the posterior external endpoint of the pelvic inlet could be located.

#### SUMMARY

1. A plea is made for concrete evidence by each investigator of the accuracy of roentgen estimates of pelvic and fetal diameters, as compared with easily measurable diameters on museum specimens or obstetrical patients at laparotomy. General knowledge of their accuracy should increase the utilization of such valuable prenatal aids as roentgen pelvimetry and cephalometry.

2. Each of the popular methods of obstetrical roentgen mensuration has an accuracy which is generally adequate for clinical purposes.

3. Two mathematical procedures for the production of precise estimates from stereoscopic films taken by a nonprecision x-ray machine, are given.

4. In our hands, the Hodges graphic, the precision, and the stereoroentgenometric methods

have proved almost equally good in the production of precise estimates of maternal pelvic and fetal diameters. The footpoint method has shown variations in precision but has very definite possibilities. The Thoms and the Hodges lateral methods for measurement of anteroposterior pelvic diameters are generally quite accurate, but correct placement of the lead ruler in the former is highly essential to precision, and pelvic asymmetry precludes consistent precision with either method. The Thoms inlet view has furnished us with precise estimates of transverse pelvic diameters only when we have been fortunate in approximating the level of the pelvic inlet in the selection of the posterior external bony landmark.

We acknowledge with gratitude our indebtedness to Dr. Paul C. Hodges for valuable aid and suggestions throughout our studies in obstetrical roentgenography. The close co-operation of the Division of Roentgenology of the Johns Hopkins Hospital, and especially that of Mr. James C. Fletcher, its chief technician, has made it possible for us to employ several roentgen techniques and to prove the accuracy of each.

#### BIBLIOGRAPHY

1. BALL, R. P. Roentgen pelvimetry and fetal cephalometry. *Radiography & Clinical Photography*, 1935, 11: 11-17.
2. Idem. Roentgen pelvimetry and fetal cephalometry including description of the pelvcephalometer. *Surg., Gynec. & Obst.*, 1936, 62: 798-810.
3. Idem. Pelvcephalometer. *Radiology*, 1938, 31: 188-197.
4. BAUDELOQUE, J. L. *L'art des accouchements*, 1789, pp. 76-90.
5. BUCHNER, E. F. Undistorted radiography in obstetrics. *J. Tenn. M. Ass.*, 1935, 28: 30-31.
6. CLIFFORD, S. H. The x-ray measurement of the fetal head diameter in utero. An accurate technique by means of stereoroentgenometry. *Surg., Gynec. & Obst.*, 1934, 58: 726-736.
7. Idem. The stereoroentgenometric method of fetometry and pelvimetry with special reference to its obstetrical application. *West Virginia M. J.*, 1935, 31: 3-11.
8. DIPPEL, A. L. The diagonal conjugate versus x-ray pelvimetry. *Surg., Gynec. & Obst.*, 1939, 68: 642-647.
9. FRIEDMAN, L. J., and EUPHRAT, E. J. Roentgen pelvimetry, a simplified parallax method. *Am. J. Roentgenol.*, 1939, 41: 541-544.
10. HODGES, P. C., and LEDOUX, A. C. Roentgen ray pelvimetry, description of a simplified stereoroentgenographic method. *Am. J. Roentgenol.*, 1932, 27: 83-95.
11. HODGES, P. C. Roentgen pelvimetry and fetometry. *Am. J. Roentgenol.*, 1937, 37: 644-662.
12. Idem. Personal communication.
13. JOHNSON, C. R. Stereoroentgenometry, with a description of a new method for mensuration by means of roentgen ray. *Am. J. Surg.*, 1930, 8: 151-163.
14. Idem. Pelvimetry by stereoroentgenometry. *Am. J. Roentgenol.*, 1937, 38: 607-619.

5. Motow H. C. A new method of roentgen pelvimetry. *Am. J. Roentgenol.*, 933, 30. -114.
6. Motow H. C., and Swenson, P. C. The use of the roentgen-ray in obstetrics. Chap. 10, *Golden, Ross. Diagnostic Roentgenology* New York. Thomas Nelson & Sons, 936.
7. SCHULMAN, E. A. The size and shape of the pelvic inlet as determined by direct measurement. *Am. J. Obst. & Gynec.*, 936 31 832-835.
8. THOMAS, H. Outlining superior strait of pelvis by means of x-ray. *Am. J. Obst. & Gynec.*, 92 4. 57-63.
9. Idem. *The Obstetric Pelvis*. Baltimore The Williams & Wilkins Co. 915.
10. THOMAS, H. and WILSON H. M. Roentgen methods for routine obstetrical pelvimetry. *Yale J. Biol. & Med.*, 938, 10 437-444.
11. Idem. The practical application of modern pelvimetric methods. *Yale J. Biol. & Med.*, 1939, 39-186.
12. THOMAS, H., HOWARD, L. P. and HAMILTON, W. F. A roentgen pelvimeter simplifying Thomas' method. *Radiology*, 938, 31 584-586.
13. VASILEV, H. J. Note préliminaire sur une méthode nouvelle de radiopélvimétrie. *Compt. rend. Soc. d'obst. de gynéc. et de pécicat. de Par.* 900, 1924.
14. WATSON, H. J. Intrauterine roentgen cephalometry and pelvimetry. *Am. J. Roentgenol.* 193 1. 768-769.

# CONSTRICTIVE OCCLUSION OF THE SUPERIOR VENA CAVA

## Report of Three Cases in Which the Patients Were Treated Surgically

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**C**ONSTRICTIVE occlusion of the superior vena cava with or without accompanying thrombosis of the vessel is fortunately a very rare occurrence. Ochsner and Dixon, in 1936, after an exhaustive study of the world literature, were able to collect only 120 cases of thrombosis of the superior vena cava. Erlich, Ballou, and Graham, in 1934, found only 309 cases of all types of obstruction to the superior vena cava. Hinshaw and Rutledge have recently added to this list 20 cases in which the patients were examined personally by them at the Mayo Clinic. The causation of the occlusion in 4 of their cases was thought to be constriction of the vessel, with associated thrombosis resulting from inflammatory changes in the mediastinum.

The collected cases of thrombosis of the superior vena cava have been classified by Ochsner and Dixon as to causation in the following manner: 44, 36.6 per cent, resulted from phlebitis, 35, 29.1 per cent, from external compression, 28, 23.3 per cent, from mediastinitis, and in 13, 10.8 per cent, the cause either was not stated or was unknown. Of the 44 cases of phlebitis and associated thrombosis, 20 were classified as idiopathic, 10 were associated with cardiac disease, 12 were cases of syphilitic phlebitis, 4 were tuberculous phlebitis, 7 were pyogenic phlebitis and 1 was traumatic phlebitis. External compression was thought to be the cause of thrombosis in 35 cases. Of these 35, 18 were associated with mediastinal neoplasms and the remainder with aneurysms. Of the 28 cases in which there was antecedent mediastinitis, syphilis was the etiologic agent in 11 cases, tuberculosis in 10 cases, trauma in 1 case, and in 5 the causation of the mediastinitis was unknown. The underlying etiologic agents named in order of their frequency in the production of thrombosis of the superior vena cava in the reported cases are syphilis, tuberculosis, cardiac disease, pyogenic infections, and trauma.

The average age of the patients in the reported cases was 43.6 years. The disease occurred approximately twice as frequently among male patients as among female patients.

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As a result of occlusion of the superior vena cava, a marked increase in the venous pressure in the upper half of the body occurs, with the production of a characteristic clinical picture. Edema of the face, neck, and upper extremities becomes a distressing feature. At the onset of the condition the edema may be intermittent. It decreases after the patient has been up and around and is aggravated by the recumbent position. Exercise and bending forward on the part of the patient exaggerate the edema. Edema of the eyelids may be an early sign of the disease. Sudden death has been attributed to edema of the glottis by Rauth. Cyanosis, particularly of the lips and lobes of the ears, may be a prominent feature. Suffusion of the conjunctival vessels and dilatation of the retinal veins on funduscopic examination are again evidence of venous stasis. Dyspnea, occurring as a result of chemical changes in the blood, is present early. Stasis in the cerebral vessels results in congestion of the cerebrum and increased pressure of the cerebrospinal fluid. Headache may be the presenting symptom. In one of our patients typical jacksonian epilepsy developed, as occurred also in the case reported by Chiray and Semelaigne. In Samek's case, psychosis developed. Other symptoms, such as vertigo, somnolence, deafness, tinnitus, epistaxis and visceral disturbances, have been reported. Pleural effusion may occur. Occlusion of the superior vena cava manifests itself objectively in increased venous pressure, collateral diversion of the blood stream, and delayed circulation time. Fischer has divided obstructions into three anatomical types together with the number of times each type occurred: (1) obstruction below the orifice of the azygos veins, 31 of 166 cases, (2) obstruction including the azygos veins, 121 of 166 cases, (3) obstruction above the orifice of the azygos veins, 14 of 166 cases. Carlson (3) demonstrated experimentally in dogs that obstruction of the superior vena cava above the azygos veins was well tolerated, whereas obstruction below those veins was fatal for the 2 animals in which it was attempted. Occlusion of the azygos system and superior vena cava could be successfully accomplished if carried out in two stages. Carlson found that an early return to relatively normal

5. MOLLOY H. C. A new method of roentgen pelvimetry. *Am. J. Roentgenol.* 913, 30 111.
6. MOLLOY H. C., and SWINSON, P. C. The use of the roentgen-ray in obstetrics. Chap. 10, Golden, Ross. *Diagnostic Roentgenology* New York Thomas Nelson & Sons, 916.
7. SCHUMLOCK, E. A. The size and shape of the pelvic inlet as determined by direct measurement. *Am. J. Obst. & Gynec.*, 915, 3 812-815.
8. THOMAS, H. Outlining superior strait of pelvis by means of ray. *Am. J. Obst. & Gynec.*, 92, 4 57-563.
9. Idem. *The Obstetric Pelvis*. Baltimore. The Williams & Wilkins Co. 915.
10. THOMAS, H., and WILSON, H. M. Roentgen methods for routine obstetrical pelvimetry. *Yale J. Biol. & Med.*, 918, 10 437-444.
11. Idem. The practical application of modern pelvimetric methods. *Yale J. Biol. & Med.*, 919, 79-116.
12. TORREY, R., HOLMES, L. P. and HAMILTON, W. F. A roentgen pelvimeter simplifying Thomas' method. *Radiology*, 1938, 3 514-516.
13. VARETTE, H. Note préliminaire sur une méthode nouvelle de radiopélvimétrie. *Compt. rend. Soc. d'obst. de gynéc. et de pécédit. de Par.* 900, 121.
14. WALLON, H. J. Intrauterine roentgen cephalometry and pelvimetry. *Am. J. Roentgenol.* 93, 15 768-769.

associated with neoplasia, the rate was 94.4 per cent and in 24 cases those in which mediastinitis was present, 22 patients died. Of the 44 patients who had phlebitis, 32 died. In addition to this terrific mortality it is probable that those patients who survived were incapacitated for long periods. As is evident, the prognosis is dependent to a large degree on the etiological agent causing the thrombosis. Until relatively recently, there has been very little in the way of treatment to offer these unfortunate people. Phlebotomy with removal of several hundred cubic centimeters of blood may be temporarily beneficial. Antisyphilitic therapy is of great value for those patients who have syphilitic endophlebitis or mediastinitis. Roentgen therapy is of no benefit unless an associated radiosensitive tumor is present. Skillern, in 1917, made the suggestion that decompression of the thorax might be of some benefit in those cases in which there was increased intrathoracic pressure, resulting, for example, from a neoplasm or aneurysm. Ehrlich, Ballou, and Graham reported a case in which mediastinal decompression aided a patient suffering from superior vena caval obstruction caused by mediastinal Hodgkin's disease. The patient operated on by Ochsner and Dixon derived great benefit from the separation of adhesive bands surrounding the thrombotic superior vena cava. We wish to report 3 cases in which the patients have been operated on at the Mayo Clinic recently. Two of these had what was believed to be thrombosis associated with constricting bands, and the third had only constriction as a result of tuberculous mediastinal glands.

One case (Case 2) has been reported previously by Rutledge and Gray. It is repeated herein for the sake of completeness, since additional follow-up notes have been made.

#### REPORT OF CASES

**CASE 1** A housewife, aged 37 years, came to the clinic in May, 1939. She had been perfectly well until the onset of her present illness, except for injuries sustained in a minor automobile accident in November, 1937. At that time she had received a slight contusion of the anterior thoracic wall which inconvenienced her for only one day. In September, 1938, she had begun to complain of a sensation of fullness in her throat and a slight swelling of the face. The symptoms were exaggerated by exercise and by bending forward. She gradually became worse and was unable to sleep, unless she was propped up on two or three pillows, because of the sensation of tightness in her thorax and throat. Dyspnea and a mild degree of cyanosis made their appearance. Three months prior to her admission to the clinic she had noted that the veins of her chest, arms, and face were becoming more prominent.

On physical examination edema (graded 3 on the basis of 1 to 4) of the eyelids, neck, and upper extremities was found to be present. The veins of the thorax were dilated and

prominent as were the venules along the anterior costochondral margin (Fig. 1). A soft enlarged node was palpable in the left axilla. Roentgenologic examination of the thorax revealed a shadow on the right, above the arch of the aorta, which was interpreted as being an accentuation of the shadow cast by the vena cava. The direct venous pressure in the right arm was 336 millimeters of water and in the left, 330 millimeters. The remainder of the physical examination and laboratory tests revealed no abnormal findings.

A clinical diagnosis of superior vena caval obstruction probably associated with mediastinal fibrosis was made.

It seemed advisable to secure a specimen of the enlarged node in the left axilla for biopsy before mediastinal exploration was undertaken. On May 5, 1939, the node was removed through a small incision in the left axilla. The pathologist reported it to be an inflammatory lymph node.

On May 23, 1939, exploratory mediastinotomy was carried out under anesthesia produced intratracheally with gas and ether. Exposure was accomplished by the usual U shaped incision, the right breast being reflected upward and medially. The pectoralis major muscle was cut across over the third interspace anteriorly, the pleural space opened and the ribs were reflected with the retractor. A hard tumor-like structure could be felt in the region of the superior vena cava, through the mediastinal pleura. This started just proximal to where the superior vena cava dipped behind the pericardial fold and extended upward for approximately 4.5 centimeters, it was roughly 2.5 centimeters in diameter and almost bone hard in its consistency. More definite exposure being obtained by incising the mediastinal pleura, a band like structure was observed which seemed to be constricting the vena cava. This was split longitudinally to a depth of approximately 3 millimeters, and a portion was sent to the laboratory for histopathological examination. It did not seem advisable to carry the dissection further, lest uncontrollable hemorrhage result. Anatomical closure of the incision was accomplished after reflation of the lung. The tissue which was removed proved to be fibrous inflammatory tissue. A transfusion of 500 cubic centimeters of citrated blood was administered slowly during the operation.

Immediately after operation the patient was placed in an oxygen tent, where she remained for 4 days. Roentgenological and physical examination of the thorax on May 31, 1939, showed evidence of the presence of fluid in the base of the right lung. However, as the fluid was thought to be of small amount and as the patient was having no respiratory difficulties, thoracentesis was not performed. Determinations of direct venous pressure on May 27 and April 6 were 250 millimeters of water. The patient progressed unusually well and was dismissed from the hospital on the seventeenth postoperative day. She left for her home, a distance of approximately 800 miles, on the twenty-first postoperative day.

Her referring physician was kind enough to keep us informed as to her subsequent progress. On July 14, 1939, he found her venous pressure to be 240 millimeters of water and on July 17, 253 millimeters. She had only a slight remaining fullness of the face and was able to lie flat in bed without the choking sensation which had been her chief complaint. The patient wrote that she was "beginning to feel like her old self again."

**CASE 2** The patient, a coal miner, aged 27 years, first registered at the clinic in January, 1939. He complained of swelling and flushing of the face which had been noticeable for about 14 months. He had had several attacks of pneumonia before he was 11 years of age. He stated that on November 11, 1937, he had suddenly noticed that if he used his arms actively or stooped, his face became flushed



venous pressure occurred in dogs in which obstruction had been accomplished above the orifice of the azygos veins, whereas in those with occlusion of both vena cava and azygos vein high venous pressure was maintained for long periods.

The collateral circulation, following occlusion of the superior vena cava, has been described by various investigators, such as Hallett, Fischer, Carlson (3), Blaslogame and Hinshaw and Rutledge and others. On the development of an efficient collateral circulation depends the future health of the patient and his ability to return to a gainful occupation. The anastomotic route utilized is determined largely by the situation of the occlusion, as has been brought out by Carlson. The systems available for shunting the blood around the obstructing lesion in the vena cava may be divided into a superficial system and a deep system. The superficial veins include the thoraco-epigastric, superficial epigastric, and the superficial plexus of veins of the thorax and abdomen, and the deep veins involved are the internal mammary azygos, hemiazygos, accessory hemiazygos, anterior and posterior mediastinal, intercostal, pericardophrenic, phrenic, superior and inferior epigastric, lumbar and deep veins of the back. Carlson (4) demonstrated experimentally in dogs that when obstruction above the junction of the vena cava with the azygos vein occurred, the azygos system was a very important path for the return flow of blood to the heart and that the abdominal collateral vessels were not well developed. In the presence of obstruction, including the azygos vein, the flow of blood in the remainder of the azygos system is evidently reversed and the superficial and deep abdominal collateral vessels carrying blood to the femoral and iliac veins or to the inferior vena cava are therefore much more prominent than normally.

Study of the collateral channels developed will enable the surgeon to localize the obstruction in a large percentage of cases, as has been emphasized by Hinshaw and Rutledge. They stated that in the presence of obstruction occurring above the level of the orifice of the azygos veins, a marked plexus of large veins may be seen over the sternum, often clearly connecting with the perforating branches of the internal mammary vein. It is apparent that the blood is seeking a route to the intercostal vessels and thence to the azygos system. Since this is a relatively efficient route of communication venous pressures are not so high and symptoms not so severe as in the instances in which other routes are necessary.

If the superior vena cava and its azygos tributaries are obstructed, it becomes necessary for

the blood from the upper half of the body to be returned to the heart through the inferior vena cava. In patients who have such obstruction, large dilated vessels are seen extending from the thorax to the lower parts of the abdomen and groin. There is a reversal of the flow of blood in these vessels which is easily demonstrable. The blood in a segment of vein is pressed out, and both ends of the segment are compressed by the index fingers. Release of the lower finger causes the vein to fill slowly or not at all, whereas on release of the upper finger the vein refills almost instantly. Since this collateral route to the inferior vena cava is long and difficult, venous pressures are high and symptoms are marked. Occlusion of the superior vena cava below the termination of the azygos system manifests itself clinically in a similar way.

Hinshaw and Rutledge have called attention to the value of thorough inspection of the thorax for those patients suspected of having mediastinal lesions. They have noted small, superficial, very tortuous groups of dilated venules which make their appearance along the anterior costochondral margins of patients who have obstructing lesions within the mediastinum. These differ in appearance from the large dilated varicosities seen over the thoracic wall, and may be the first objective signs of mediastinal disease hence their great clinical importance. Their presence is sufficient indication for a thorough roentgenological study of the thoracic cavity.

Laboratory aids in the diagnosis include estimations of direct venous pressure, determinations of the circulation time, and, of course, roentgenograms of the thorax. It is particularly important to follow the direct venous pressure of these patients for whom surgical intervention is contemplated. We believe that only those individuals who show progressive increases in their venous pressures over a period should be subjected to mediastinotomy. The circulation time, as measured by the dehydrocholic acid (decholin) method, will be found to be prolonged in the presence of obstruction of the superior vena cava, because the blood is compelled to take a circuitous route in its return to the heart. The value of making roentgenograms of the thorax need not be mentioned.

We are again indebted to Ochsmere and Dixon's excellent review of the literature for the mortality figures for patients suffering from thrombosis of the superior vena cava. Of the 120 collected cases, 85 patients died. In those cases in which thrombosis of the superior vena cava was caused by aneurysm the mortality rate was 73.3 per cent in those in which the condition was



Fig 1 Case 1 Infra red photograph showing marked tortuosity of the superficial veins of the neck and thorax

veins of the right and left arms were, respectively, 294 and 276 millimeters of water, whereas the pressure in the left greater saphenous vein measured only 48 millimeters of water. Reactions to the flocculation test for syphilis were negative. Results of other routine laboratory tests added nothing of interest.

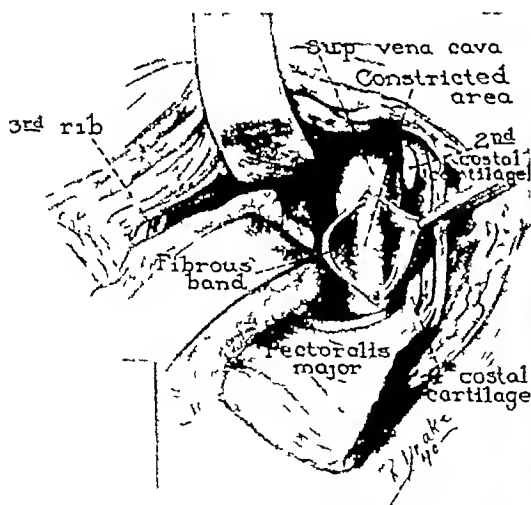


Fig 3 Artist's conception of the release of an inflammatory constricting process which had practically completely occluded the lumen of the superior vena cava below the orifice of the azygos veins. The constricted area has been released by separating the fibrous band. A U shaped incision beneath the breast may give better exposure and cosmetic results than that shown by artist.



Fig 2 Case 2 Infra red photograph showing marked dilatation and tortuosity of the veins of the chest, arm, and neck.

The diagnosis of incomplete superior vena caval obstruction was made. It seemed best to follow the patient's progress a short time by means of determinations of venous pressure, since there had not been much progression of the symptoms since their onset.

The patient returned to the clinic within one month, as had been requested of him. His symptoms had definitely progressed and one week before his return he had had an acute episode of edema. His collar size had increased from 14½ to 16¼ inches (35 to 40 centimeters). The direct venous pressures in both the right and left arms were 394 millimeters of water. Because of the progression of symptoms it was deemed advisable to explore the region of the superior vena cava.



Fig 4 Case 3 Infra red photograph showing the distention of the right and left external jugular and right and left cephalic veins, together with generalized venous tortuosity.

and swollen. At first these symptoms subsided shortly after he stopped such activity but within a month they seemed to be present continuously. When he attempted to work, the swelling increased and he noticed bluish discoloration of the face and neck. In April, 1938, he first noticed enlargement of the veins of his neck, chest, and arms. These had continued to enlarge to the time of his admission. In December, 1938, the patient had to stop work because of sensation of choking when he attempted to do anything strenuous. Edema of the lower extremities had not been present and he had no other complaints.

On physical examination at the clinic the patient's face and neck appeared to be flushed and swollen. Slight activity such as bending over several times, aggravated the symptoms. There was marked distention of the veins of his chest, arms, neck (Fig. 1) and especially of the angular veins of the face. The direction of blood flow in the veins was toward the umbilicus. The physical observations referable to the heart were not remarkable. Roentgenological examination of the thorax revealed evidence of slight thickening of the soft tissues about the vertebrae on the left side and exaggerated pulmonary markings, but did not reveal any calcification of the pericardium. The electrocardiographic tracing was that of a normal heart. The direct venous pressure in the right arm was 33.5 millimeters of water and in the left, 34.5 millimeters. Normal venous pressure is between 40 and 30 millimeters of water. The pulmonary circulation time, measured after the administration of dehydrocholic acid preparation (dechofin) as 29 seconds. The average normal time is about 14 seconds. Results of other laboratory tests were negative.

It was believed that the patient was suffering from obstruction of the superior vena cava between the azygos vein and the entrance of the vena cava into the right auricle, possibly postinflammatory condition. Roentgen therapy was given, and the patient was sent home for one month.

On his return on February 2, 1939, the patient stated that his condition was about the same, but that in addition to the previously mentioned complaints, he had had three attacks of an jerking movements of the left arm and leg which had lasted about one minute each. He did not lose consciousness when these episodes occurred. Roentgenological examination of the skull and examination of the eyes with fundoscope revealed nothing abnormal. On neurological consultation the attacks were thought to be Jacksonian seizures which probably had a vascular basis. The direct venous pressure in the right arm was 42.6, in the left, 41.6, and in the right ankle, 0.2 expressed in millimeters of water. After consultation, it was decided that in view of the progression of the condition, the patient was entitled to surgical exploration.

Exposure as accomplished by making an incision from the upper portion of the anterior axillary line to the supra-sternal notch (Fig. 2). The skin and subcutaneous tissues overlying the right pectoralis major muscle was reflected upward and down on the line between the two points, and

linear incision was made across the pectoralis major muscle over the third rib and cartilage. The medial point of the incision through the muscle as then carried downward for approximately 3 inches (7.6 centimeters) along a line which was about 1 inch (2.5 centimeters) from the insertion of the muscle. The triangular pieces of muscle were then reflected downward and outward and approximately centimeters of the third rib, together with approximately 3 centimeters of the costosternal cartilage of this rib, as removed. The cartilages of the second and fourth ribs were divided to permit greater exposure and dissection as then carried down to the pleura. The pleura was reflected laterally and extrapleural exposure of the

mediastinal structures was accomplished with some difficulty because of the presence of moderate quantity of fibrous tissue in this region. A small rent in the pleura allowed the right lung to collapse, and greater visualization of the mediastinal structures as obtained. Beginning about 2.5 centimeters above the pericardial reflection, there was an extremely hard tumor within the lumen of the superior vena cava, approximately 3 centimeters in its lowest diameter the lowermost portion of this mass extended beneath the pericardium. Evidence of extraluminal translocation was not found. An elongated constricting band, approximately centimeters in width, which compressed the superior vena cava, was divided so that the vena cava dilated at the point of previous constriction (Fig. 3). A small lymph node from the tissue immediately adjacent was removed and sent to the pathological laboratory for histopathological examination. It was found to be inflammatory. A small portion of the constricting band as removed and this also as found to be inflammatory tissue. Because the obstructing process was entirely within the superior vena cava and could not be removed, it was thought best to discontinue the exploration. The small rent in the pleura was closed, the right lung reexpanded by means of positive pressure, and aseptic closure of the wound was accomplished.

For the first 5 days immediately after the operation there was considerable swelling of all of the soft tissues of the upper portion of the thorax, neck, and arms, particularly the tissues of the left arm. This as so marked that it was impossible for the patient to flex the left arm. The

venous pressure in the left arm during this period was higher than any pressure the manometer could register, that is more than 90 millimeters of water. After the first week the swelling gradually subsided and the pressure within the veins of the arm decreased correspondingly. At the time of the patient's dismissal from the clinic, which happened on the thirty-second postoperative day, direct venous pressure of the arm had decreased to 30 millimeters of water. The veins on the upper portion of the thorax were much less prominent and in general the patient had remarkably improved.

The patient returned to the clinic for re-examination in June, 1939, as had been requested of him. His improvement had continued and for a month he had been able to return to somewhat less strenuous job at the coal mine. He had experienced no more Jacksonian seizures and was practically free of edema of the face and arms except after rather marked exertion and bending forward. The direct venous pressure in the right arm measured 27.8 millimeters of water. This patient was considered to have achieved an excellent functional result.

CASE 3. A mechanic, aged 33 years, was first seen at the clinic in March, 1939. He stated that for the past 9 months there had been intermittent swelling of his face, neck, and arms, occurring after exertion. Cyanosis of the lips, lobes of the ears, and fingernails could accompany the edema. The symptoms were relieved by rest and they had not progressed much in severity. At times the attacks are accompanied by hoarseness and dyspnea. The patient's physician at home had made a presumptive diagnosis of obstruction of the superior vena cava and had removed gland from the left axilla which proved to be inflammatory in nature.

On physical examination, slight degree of edema of the face and neck was noted. After the patient had exerted, the edema became much more marked, and distention of the right and left external jugular and right and left cephalic veins became very apparent (Fig. 4). No abnormal structures could be localized in the subcutaneous on roentgenological examination. The venous pressure in the

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Fig. 5. Constriction of superior vena cava by mass of calcified tuberculous lymph nodes; left, arrow points to portion of vena cava constricted; b, section of tuberculous mediastinal lymph node. Hematoxylin and eosin stain  $\times 100$ .

On May 2, 1939, mediastinotomy was performed under gas-ether anesthesia supplemented by pentothal sodium given intravenously. Exposure was accomplished through the usual incision. A hard tumor, approximately 3 centimeters in length, was found in the region of the superior vena cava, proximal to the pericardium. On further dissection it was found that the parietal pleura was densely adherent to this, as were the other surrounding structures. These were dissected free with extreme difficulty, and constricting mass, alone hard in nature was noted. This mass was split end to end on each side so as to release the constriction at this point. It could not be definitely determined whether there was thrombosis within the vein or whether the mass was entirely extraluminal. A lymph node from the adjacent region was sent to the laboratory and found to be an inflammatory node. A small portion of the stone-hard, constricting mass proved also to be inflammatory tissue on microscopic examination. During the dissection moderate amount of hemorrhage was encountered. Plastic closure of the wound was accomplished.

On the second postoperative day the patient suffered rather severe shock and succumbed.

On postmortem examination the superior vena cava was found to be occluded to approximately 50 per cent of its normal size by pressure caused by mass of calcified tuberculous lymph nodes (Fig. 5a and b). The other anatomical diagnoses were: healed tuberculosis of the liver and spleen, accessory pancreas of the pylorus, postmortem atrophy of the cardia of the stomach, adenoma of the adrenal glands, arteriosclerosis (graded on the basis of 1 to 4), hemorrhagic edema of the lungs with bronchopneumonia, diverticulum of the sigmoid and hemorrhage (200 cubic centimeters) into the right pleural cavity.

It is of interest to consider the causation of the obstruction in the cases just presented. Causation of the thrombosis in the first case is not definitely known. It seems hardly probable that the minor injuries of the thorax which the patient sus-

tained a year previous to the onset of her symptoms could have been the cause of the mediastinal fibrosis and the thrombosis of the vena cava. It is more likely that this patient at some time had experienced tuberculosis of the mediastinal lymph nodes or nonspecific mediastinitis.

It would appear that the second patient had mediastinitis accompanying one or more of his attacks of so called pneumonia with resulting fibrosis within the mediastinum and thrombosis of the superior vena cava.

On postmortem examination it was discovered that the third patient had suffered from compression of the superior vena cava by calcified tuberculous lymph nodes, without accompanying thrombosis.

It is also of interest to speculate as to why the release of constricting bands should result in clinical benefit in those cases in which definite thrombosis occurs within the lumen of the vena cava. Duval was of the opinion that removal of the constricting perivascular tissue permits opening of the already canalized channels within the thrombus, these vessels having been previously maintained as nonfunctioning canals because of the external pressure exerted by the encapsulating perivascular cicatricial tissue.

#### SUMMARY

Three cases of constrictive occlusion of the superior vena cava in which the patients were treated by operation have been reported. In 2 of

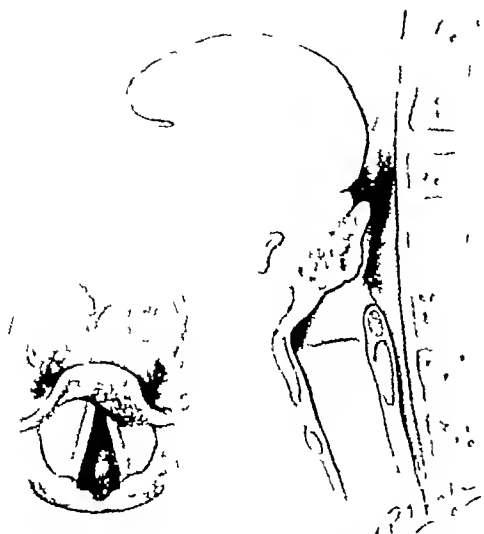


Fig 1 In a man, aged 55 years, with squamous cell epithelioma grade 4 on the posterior surface of the epiglottis extending down into the larynx and producing edema at the base of the tongue a preliminary tracheotomy was made, the epiglottis and growth were removed with diathermy, and emanation seeds were inserted into the base. Further radium seeds were inserted into the base of the tongue and epiglottis with no evidence of recurrence for 2 years

laryngoscopy when lateral or subhyoid pharyngotomy, which gives much better exposure for the larger growths, is indicated. However, many lesions, particularly the highly malignant tumors, that cannot be removed by purely surgical procedures, can be treated with the aid of suspension laryngoscopy (Figs 3 and 4)

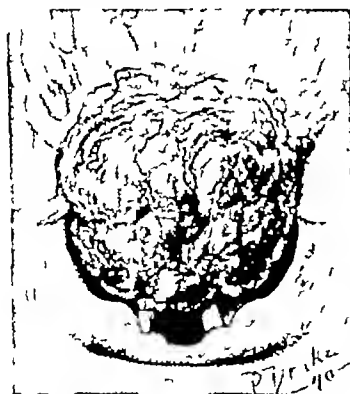


Fig 3 In a man, aged 60 years, a squamous cell epithelioma grade 4 of the epiglottis and base of the tongue was removed after preliminary tracheotomy, July 2, 1934 and radium points were inserted into the growth. The patient has had no recurrence for six years

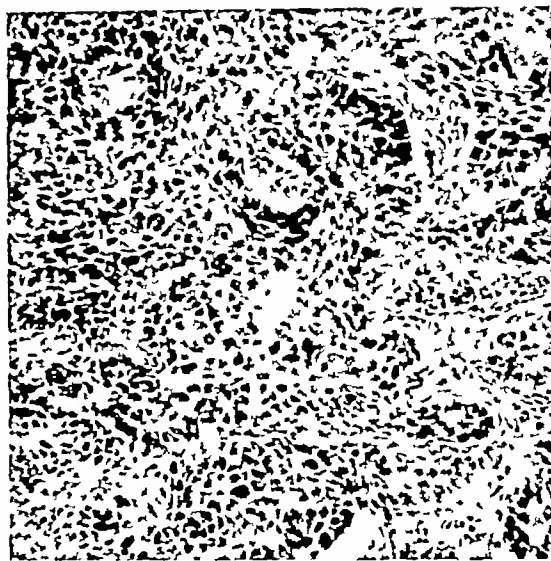


Fig 2 Photomicrograph from same case as in Figure 1  $\times 180$

In our series the intralaryngeal growths selected for treatment under suspension consisted of tumors of low grade or those of limited extent



Fig 4 Photomicrograph from same case as in Figure 3  $\times 180$

# SUSPENSION LARYNGOSCOPY IN THE TREATMENT OF MALIGNANT DISEASE OF THE HYPOPHARYNX AND LARYNX

GORDON B. NEW, M.D., F.A.C.S., and HOWARD E. DORTON, M.D., Rochester, Minnesota

**D**URING the eleven year period, 1927 to 1937 inclusive, a selected group of 38 patients with malignant disease of the hypopharynx and larynx have been treated at the Mayo Clinic with the aid of suspension laryngoscopy. Surgical diathermy and radium emanation seeds have been employed, and, in addition, external irradiation has been used at times.

While suspension laryngoscopy has been used for many years, its value in the treatment of malignant diseases of the hypopharynx and larynx is not generally known. We feel that carefully selected patients can be taken care of with less surgical risk when laryngeal suspension is employed. Immediate histological diagnosis by the fresh frozen section is an essential part of this method.

Lynch did more than anyone else in this country to perfect and stimulate interest in suspension laryngoscopy. In 1928 he reported dissection with a knife of early intrinsic laryngeal epithelioma under suspension and recommended its use in certain selected cases.

Kilham in giving the Semon lecture stated that Mayer removed an epithelioma of the epiglottis in 1914 under suspension laryngoscopy but said that such cases ought to be selected with care.

At the Mayo Clinic we have used suspension laryngoscopy for many years and feel that it has a definite place in the treatment of cancer of the hypopharynx and larynx. However the apparent lack of widespread knowledge of its usefulness is shown by a statement of Thomson in 1939 when he said, operation *per vias naturales* is now only of historical interest, though pathologically of some importance, and he attributed the occasional rare instances of cure by this route to low grade lesions of minor extent.

## SELECTION OF CASES FOR TREATMENT

Our series consisted of 38 cases of malignant disease in the hypopharynx and larynx in which

treatment had been given under suspension laryngoscopy during the years 1927 to 1937 inclusive. During this same period approximately 450 patients were operated on at the clinic for malignant disease of the larynx and hypopharynx. This brings out the fact that the cases in which treatment was given under suspension laryngoscopy are a selected group.

We have divided the cases into 5 groups depending on the location of the growth: (1) growths at the base of the tongue in the hypopharynx; (2) supraglottic growths; (3) intralaryngeal growths; (4) growths involving the lateral and posterior walls of the hypopharynx; and (5) post-cricoid growths. Some of these lesions involved two or more of these sites, but we grouped them according to the place where the major part of the tumor was situated. As each one of these various groups presented different problems, the selection of cases for treatment in this manner must be discussed individually rather than collectively.

Growths at the base of the tongue in the hypopharynx that were part of carcinomas of the body of the tongue were not considered. Only primary growths at the base of the tongue in the hypopharynx were included. Growths in this location can be of three varieties: (1) adenocarcinoma, mixed tumor type which is usually a low grade tumor; (2) highly malignant squamous cell epithelioma of grade 3 or 4 that infiltrates into the tongue and that is an active growth; and (3) squamous cell epithelioma of low grade which does not infiltrate into the tongue but is an outgrowth from the surface of the tongue. All of these lesions are best taken care of under suspension laryngoscopy because of the difficulty of obtaining a direct view of them in a satisfactory way with any other method. Only an extensive lesion or extensive metastasis would prevent treatment in this group of cases.

The supraglottic growths consisted of those which involved the epiglottis alone or those that extended into the aryepiglottic fold, base of the tongue, or lateral wall of the pharynx (Figs. 1 and 2). Care should be taken not to attempt to treat lesions in this region under suspension

From the Section on Laryngology, Oral and Plastic Surgery, the Mayo Clinic, and the Department of Surgery, the Mayo Foundation.

Read before the meeting of the Academy of Ophthalmology and Otolaryngology, Cleveland, Ohio, October 7 to 9, 1940.

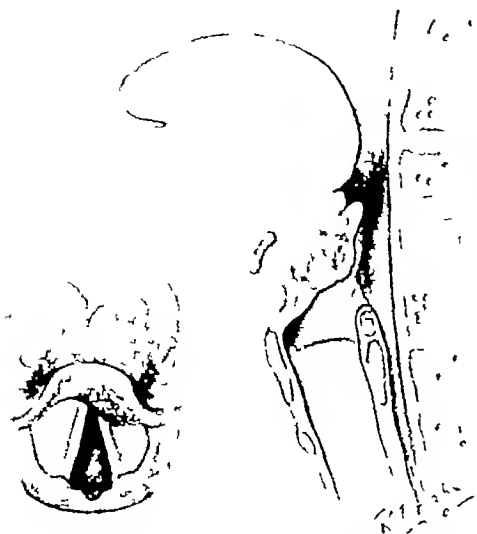


Fig 1 In a man, aged 55 years, with squamous cell epithelioma grade 4 on the posterior surface of the epiglottis extending down into the larynx and producing edema at the base of the tongue, a preliminary tracheotomy was made, the epiglottis and growth were removed with diathermy, and emanation seeds were inserted into the base. Further radium seeds were inserted into the base of the tongue and epiglottis with no evidence of recurrence for 2 years

laryngoscopy when lateral or subhyoid pharyngotomy, which gives much better exposure for the larger growths, is indicated. However, many lesions, particularly the highly malignant tumors, that cannot be removed by purely surgical procedures, can be treated with the aid of suspension laryngoscopy (Figs 3 and 4)

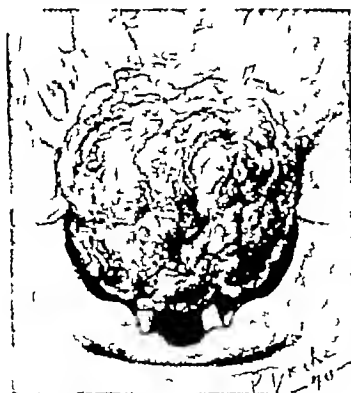


Fig 3 In a man, aged 60 years, a squamous cell epithelioma grade 4 of the epiglottis and base of the tongue was removed after preliminary tracheotomy, July 2, 1934, and radium points were inserted into the growth. The patient has had no recurrence for six years

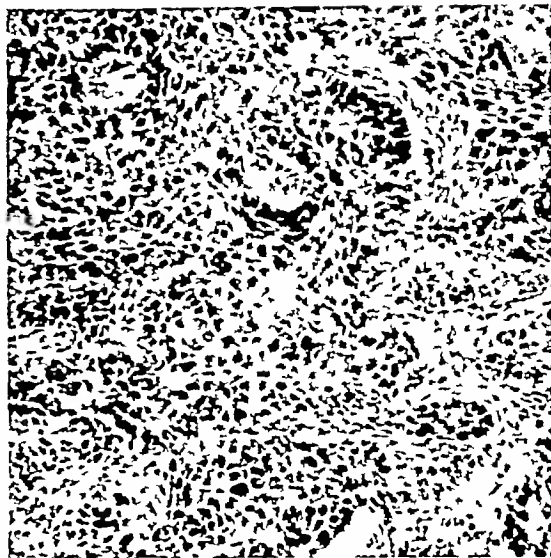


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In our series the intralaryngeal growths selected for treatment under suspension consisted of tumors of low grade or those of limited extent



Fig 4 Photomicrograph from same case as in Figure 3  $\times 180$



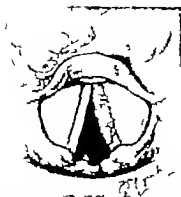


Fig. 5 In situ, aged 44 years, squamous cell epithelioma grade 1 at the base of leucoplacta along the anterior two-thirds of the left vocal cord as removed by means of surgical diathermy November 20, 1936, under suspension laryngoscopy with no recurrence for 13 1/2 years.

on the anterior two-thirds of the vocal cord frequently a thickened leucoplacta with early epithelioma was taken care of in this manner (Figs. 5 and 6). For elderly patients, particularly those with hypertension, diabetes, or bronchiectases, for whom the risk from thyrotoxy is increased, removal of the lesion by intralaryngeal methods is justified if the lesion is small, of low grade and there is no fixation of the cord.

The growths, involving the lateral and posterior walls of the hypopharynx, are usually highly malignant tumors. They can be treated by the insertion of radium seeds into the lesion as well as by external irradiation. Tumors of the highly malignant type can be treated more successfully with radium than low grade tumors; consequently small lesions of low grade should be removed with surgical diathermy.

Of the postcricoid growths only two have been treated in this series with the aid of suspension



Fig. 6. Photomicrograph from same case as in Figure 5 X 25.

laryngoscopy. In most of these cases roentgen therapy with fractional doses accomplishes as much as any local treatment of the growth. It is only in the low grade lesions that we feel that external operation by the method of Trotter in which lateral pharyngotomy is performed, gives the patient any permanent benefit.

#### REVIEW OF CASES

The average age of the 38 patients was 57.4 years. The youngest was a woman aged 20 years, who had squamous cell epithelioma grade 1 of the middle third of the vocal cord, and the oldest was a man, aged 79 years, who had squamous cell epithelioma grade 4 of the base of the tongue.

TABLE II.—HISTOLOGICAL TYPE—  
1927-1937 SERIES

| Lesion   | Histological grade | Patients |                                   | Length of life after treatment (years) |     |
|--|--------------------|----------|-----------------------------------|--|-----|
|  |                    | Total    | Living last report, no recurrence | Caused death                           | Age |
|  |                    |          |                                   | 2                                      | 1   |
| Squamous cell epithelioma                          |                    |          | 2                                 | 1                                      | 1   |
|  |                    |          |                                   |  | 1   |
| Mixed adenocarcinoma and squamous cell epithelioma |                    |          |                                   | 6                                      | 1   |
|  |                    |          |                                   | 5                                      |     |
| Squamous cell carcinoma                            |                    |          |                                   | 5                                      |     |
| Mixed tumor  |                    |          |                                   |  |     |
| Lymphoma   |                    |          |                                   |  |     |
| Fibrosarcoma                                       |                    |          |                                   |  |     |
| Total  |                    | 3        | 3                                 | 22                                     |     |

1Died of malignancy.  
1Died of carcinoma of the stomach.

TABLE I.—LOCATION OF LESION IN SERIES  
1927-1937 INCLUSIVE

| Site of Lesion                           | Patients |                                   | Length of life after treatment (years) |     |
|--|----------|-----------------------------------|--|-----|
|  | Total    | Living last report, no recurrence | Caused death                           | Age |
| Base of tongue                           | 20       |                                   |  |     |
| Supraglottic region                      |          | 5                                 | 5                                      |     |
| Intralaryngeal region                    |          |                                   |  |     |
| Hypopharynx, posterior and lateral walls |          |                                   | 1                                      |     |
| Postcricoid region                       |          |                                   |  |     |
| Total                                    | 20       | 5                                 | 6                                      | 4   |

\*Died of recurrence.

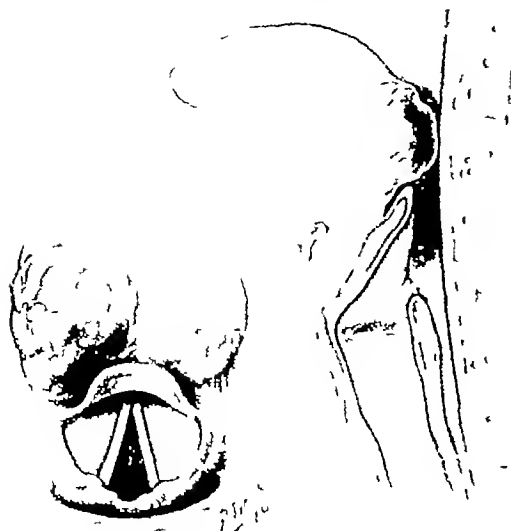


Fig 7 In a woman, aged 70 years, a lymphosarcoma of the base of the tongue at the level of the epiglottis was partially destroyed with diathermy on June 17, 1936, and radium points were inserted into the growth. She has had no recurrence for 4 years.

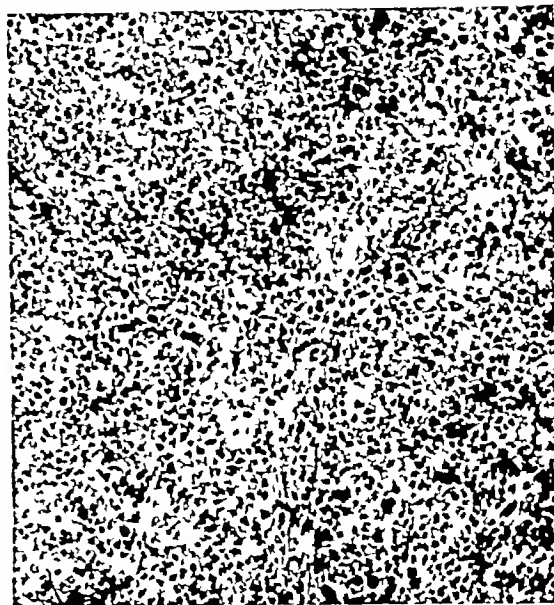


Fig 8 Photomicrograph from same case as in Figure 7. X190.

There were 4 women in this group, the ratio of males to females being 85:1. Three patients (79 per cent) had syphilis.

Ten lesions were situated at the base of the tongue, 12 were in the supraglottic region, 11 in the intralaryngeal region, 3 on the lateral and posterior walls of the hypopharynx, and 2 in the postcricoid region (Table I).

The most common symptoms in this group of cases were dysphagia and hoarseness. The symptoms, of course, depend on the location and extent of the lesion. Malignant lesions at the base of the tongue are frequently overlooked. The advanced lesions produce marked symptoms of pain, bleeding, and so forth, while the early lesions produce little discomfort. On this account, patients with epithelioma of the base of the tongue, epiglottis, and aryepiglottic fold usually have large lesions at the time of the first examination. Patients with early lesions of the supraglottic region frequently complain of a sensation of a foreign body in the throat while those with lesions on the vocal cords have hoarseness early and are frequently seen with a small lesion. Only 3 patients noticed enlarged glands in the neck, although 8 patients had enlarged glands in the cervical region at the time of examination.

#### THE METHOD OF TREATMENT

Pentobarbital sodium,  $1\frac{1}{2}$  grains (0.1 gm), was administered by mouth an hour before the opera-

tion. The larynx was cocaineized with a 10 per cent solution of cocaine, and the patient was then anesthetized with sodium ethyl (1-methylbutyl) thiobarbiturate (pentothal sodium) given intravenously. A 25 per cent solution was used. A pharyngeal tube was inserted into one of the nostrils through which oxygen was administered throughout the procedure. The pentothal sodium was administered intermittently whenever necessary.

A flat spatula attached to the suspension apparatus was employed for the lesions at the base of the tongue. For lesions of the epiglottis the spatula picked up the base of the tongue and exposed the entire epiglottis and vallecula. For intralaryngeal lesions the spatula picked up the epiglottis, and the surgeon had a direct view of the entire glottis. In all cases a specimen of the lesion was removed, a fresh frozen section was examined, and immediate diagnosis was made. Results of microscopic examination of the tissue removed are given in Table II.

In cases of carcinoma of the base of the tongue and epiglottis or aryepiglottic fold, preliminary tracheotomy was performed. After recovery the laryngeal suspension was done, and treatment was performed. For growths involving the base of the tongue (Figs 7 and 8), radium emanation seeds were inserted into the lesion after the use of surgical diathermy. If the lesion was of limited extent, the entire treatment was completed with surgical



Fig. 9. 1. man, aged 45 years, squamous cell epithelioma grade 4 of the entire base of the tongue and large metastatic mass measuring 3 by 2.5 by 2.5 centimeters in the cervical region. As treated under suspension laryngoscopy August 1933 and radon seeds are inserted into the growth. This is followed by roentgen treatment applied externally to the neck. The patient is alive and well and without recurrence seven years after treatment.



Fig. 10. Photomicrograph of specimen from the same case as in Figure 9.  $\times 80$ .

diathermy alone. The supraglottic lesions were destroyed with a long protected diathermy point. This is a long needle covered with Duco varnish so that only the distal end of the needle is exposed. The epiglottic growths were removed piecemeal or in one piece with the Bovie surgical diathermy unit. The intralaryngeal lesions were removed with the diathermy point. No attempt was made in the primary laryngeal lesions to use radium in addition to diathermy except in unusual circumstances, for we felt that lesions extensive enough to need radium in addition to diathermy are better treated by means of thyrotomy.

In addition to treatment under suspension radium or roentgen rays were applied to the outside of the neck, especially in cases of highly malignant growths at the base of the tongue.

#### RESULTS

The results of the treatment of malignant disease of the hypopharynx in the past have been very poor. The Trotter operation has produced some very striking results, but they are few. Recently fractional doses of roentgen rays as well as radium used externally have been of considerable benefit. Lenz in discussing Martin's paper reported 31 cases of hypopharyngeal malignancy; 69.3 per cent. of his patients were apparently free of disease, but the length of time these patients have lived since treatment was not stated. Four of these patients had growths involving the epiglottis.

Of the 27 patients with malignant disease of the hypopharynx including the base of the tongue (Figs. 9 and 10) supraglottic region, lateral and posterior walls of the hypopharynx, and post-cricoid region we were able to trace 26, and 14, or 51.8 per cent. of the patients who were traced were alive and well.

Of the 11 patients with intralaryngeal lesions, 10 were traced and 9 or 80 per cent. were alive and without recurrence. These patients had small, low grade lesions which account for this very high percentage of cures.

TABLE III.—THREE AND FIVE YEAR SURVIVALS

| Period after treatment | Patients treated | Patients traced | Survived beyond indicated period |         |
|------------------------|------------------|-----------------|----------------------------------|---------|
|                        |                  |                 | Number                           | Percent |
| or more years          |                  | 31              |                                  |         |
| 1 or more years        | 17               | 7               | 10                               | 29      |

\*The 3 year group comprises the patients treated or more years prior to the time of inquiry than 10, 15, 20 or earlier; the 5 year group comprises the patients treated or more years prior to the time of inquiry than 10, 15, 20 or earlier.

Nine of the traced patients, or 25 per cent, died of cancer, the majority within a year and a half of the final treatment. One of the group now dead lived 7 years, and another of the group, 6½ years.

There was 1 postoperative death, the patient died of bronchopneumonia 8 days following treatment of an epithelioma at the base of the tongue. The patient did not have a preliminary tracheotomy.

The 3 and 5 year survivals are shown in Table III. Of 31 patients treated and traced for 3 or more years (operations were performed in 1936 or before), 23, or 74 per cent, lived more than 3 years. Of 17 patients treated and traced for 5 years (operations were performed in 1934 or

earlier), 10, or 59 per cent, lived more than 5 years. In the series there were 3 patients who have lived more than 9 years following treatment, and all of these are living at the time of this report (1940).

#### REFERENCES

- 1 KILLIAN, GUSTAV Suspension laryngoscopy Clin J, 1915, 44 89-104
- 2 LENZ, MAURICE Discussion Radiology, 1940, 34 161-163
- 3 LYNCH, R. C. Cancer of the larynx Illinois M J, 1928, 54 40-44
- 4 THOMSON, ST. CLAIR The history of cancer of the larynx J Laryngol & Otol, 1939, 54 61-87
- 5 TROTTER, WILFRED Malignant disease of the hypopharynx and its method by excision Brit M J, 1932, 1 510-513

# THE DEMONSTRATION OF MYCOBACTERIUM TUBERCULOSIS IN ANORECTAL ABSCESS

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**A**n abundant literature is available reporting various diagnostic laboratory procedures for the demonstration of *Mycobacterium tuberculosis* in fistula in ano. Recently Buie Smith, and Jackman reviewed the subject calling attention to the almost universal failure to demonstrate the organism by direct staining methods. They recommended guinea pig inoculation. Quite recently Joynt confirmed the general conclusions of previous writers and employed culture methods in place of the guinea pig. In relation to the antecedent condition, anorectal abscess, demonstration of the organism by direct microscopical methods has not been reported with any important degree of success. In institutions where patients are continuously under observation we may anticipate the spontaneous rupture of these abscesses by aspirating the contents. During the past 9 years we have successfully aspirated 16 of a total of 20 abscesses under observation.

## CLINICAL MATERIAL

This report is concerned with the investigation of 22 abscesses from 9 patients. All patients furnishing material for examination had positive sputum except 1 whose pulmonary history was unknown, as the specimen was sent in by an outside physician. One patient had 3 distinct abscesses form over a period of 1 year. Another had 2 abscesses during a 4 months' period.

Sixteen abscesses were successfully aspirated. Rupture during preparation for aspiration occurred 4 times and spontaneous rupture occurred from week to 4 months before investigation in 5 instances.

## PROCEDURE

The syringe and needle No. 6 were sterilized at 220 degrees C. dry heat for 1 hour. The investigation of the material was made with the dilution-flotation procedure (3) and guinea-pig inoculation. All animals were tested before they were used with 0.1 cubic centimeter purified protein derivative second strength. The same dose was given as a diagnostic test on the twentieth day after inoculation.

From The Pottinger Sanatorium, Monrovia, California

The pus diluted 10 times with 0.5 per cent sodium hydroxide was shaken in a strong shaker for 5 minutes and set at 37 degrees for 1 hour or in case contaminating organisms were present, for 2 hours. Thorough homogenization was accomplished by 10 minutes shaking. The centrifuge was employed at 1000 revolutions per minute for 2 minutes, to throw down undigested tissue fragments. The upper third of the solution was pipetted off, placed at 55 degrees C. for 30 minutes to complete the digestion process and used for dilution-flotation. The final dilution with distilled water was made so that the amount of the original material contained in the fraction would be diluted 100 times. (On account of the high protein content of this type of material it is necessary to dilute to a much greater degree than is necessary in the case of sputum.) From 0.5 to 1 cubic centimeter of xylol was added, and the mixture shaken for 10 minutes. Films were made from the xylol layer by means of a capillary pipette. The exact number of organisms found in a 10 minute search was recorded if present to the extent of one in two fields or less.

For guinea pig inoculation the remaining two-thirds of the digested specimen was employed. It was neutralized with 3 per cent hydrochloric acid in the presence of brom-thymol-blue, and injected subcutaneously in divided dosage in 2 or more regions. (If all the inoculum is given in one region, pyogenic ulceration may occur early and expel the organisms before infection takes place. Ulceration of all inoculation sites in case of divided dosage is a rare event.) We had but 1 early pyogenic abscess in the series. The animal, however was positive. In 9 animals the inoculation was made intraperitoneally. Not a single animal was lost by death due to other causes.

## RESULTS OF INVESTIGATION

Of 20 abscesses and recently formed sinuses investigated 4 showed from 2 to 1 organisms per field, so that confirmation by inoculation was not needed. The results obtained by dilution-flotation and guinea-pig inoculation of material obtained from the remaining 16 abscesses are tabulated in Table I. The table presents 3 groups of

TABLE I—FINDINGS BY DILUTION-FLOTATION AND GUINEA-PIG INOCULATION IN 18 ANORECTAL ABSCESSES AND RECENTLY FORMED FISTULAS IN 14 KNOWN TUBERCULOSIS PATIENTS

| Specimens                            | No of examinations | Average amount c.cm | D.F. +<br>G.P. + | D.F. -<br>G.P. - | D.F. -<br>G.P. + | D.F. +<br>G.P. - |
|--------------------------------------|--------------------|---------------------|------------------|------------------|------------------|------------------|
| Aspirated                            | 13                 | 2.66                | 12               | 1                | 0                | 0                |
| Ruptured at operation                | 4                  | 0.49                | 2                | 1                | 1                | 0                |
| Ruptured 4 mos. before investigation | 1                  | 0.01                | 0                | 0                | 1                | 0                |
| Totals                               | 18                 |                     | 14               | 2                | 2                | 0                |

D.F. dilution flotation  
G.P. guinea pig

results The first consists of 13 successfully aspirated abscesses averaging 2.66 cubic centimeters The second consists of 4 abscesses which ruptured into the anal canal under pressure from the speculum resulting in much loss of material and averaging 0.49 cubic centimeter of material recovered The third group represents a single specimen in which a very small amount of serous discharge was obtained from a fistulous tract which had formed 4 months previously

In the first group of successful aspirations dilution-flotation and guinea-pig inoculation were in 100 per cent agreement, 12 positive and 1 negative result In the second group of 4 abscesses rupturing under pressure, agreement resulted in 3 instances, 2 positive and 1 negative, and in the fourth instance in which only 0.05 cubic centimeter of material was obtained, dilution-flotation was negative but the guinea-pig was positive In the third group dilution-flotation was negative and the guinea-pig was positive

The total of the 3 groups shows 18 specimens in which dilution-flotation and inoculation were in agreement 16 times Fourteen specimens were positive and 2 negative It should be noted that the 2 failures by dilution-flotation occurred with materials small in amount, following spontaneous rupture

TABLE II—RANGE OF THE NUMBER OF ORGANISMS FOUND IN 18 SPECIMENS POSITIVE BY DILUTION-FLOTATION

|                                     | Times Found |
|-------------------------------------|-------------|
| 1 in 2 fields to 10 per field       | 8           |
| Organisms found in 10 minute search |             |
| 15 to 79                            | 1           |
| 1 to 14                             | 9           |

Elsewhere (3, 4) the relative sensitivity of homogenized smears counterstained with strong

methylene blue, with picric acid, and the same material treated by dilution-flotation counterstained with picric acid is given as 1, 5, 5, and 80, respectively Applying these ratios to Table II, 8 of the 18 specimens, or 44.4 per cent should be positive by Ziehl-Neelsen with methylene blue counterstain If picric acid is used, another specimen should be positive, making 9 positives in a total of 18 or 50 per cent Nine specimens should be found positive only by dilution-flotation This is the group in which the organisms are so rare that they may be found by Ziehl-Neelsen only by prolonged search of an hour or more Even with the 15-fold enrichment attained by dilution-flotation only 4 organisms were found in 1 specimen in 1 hour's search In the remaining specimens the organisms were found during the first 5 minutes' search Ziehl-Neelsen counterstained with picric acid was carried out in 7 of the 18 specimens, 4 of which, or 57.1 per cent, were positive This percentage agrees well with the probable percentage deduced from the known sensitivity ratios

The actual number of organisms found in the 9 specimens per cubic centimeter of material is small Corper established about 100,000 organisms per cubic centimeter as the lower limit of sensitivity of the Ziehl-Neelsen method and since dilution-flotation with picric acid counterstain is 80 times more sensitive, a single bacillus found in 10 minutes' search would indicate  $100,000 \div 80 = 1250$  organisms per cubic centimeter The number of organisms, 1 to 14, found in a 10 minute search would indicate the presence of 1250 to 17,500 organisms per cubic centimeter of original material investigated

#### EVALUATION OF STUDY

In view of the unprecedented success with which we have demonstrated Mycobacterium tuberculosis in this series of abscesses, we wish to point out the causes of failure of earlier workers First, the selection of the optimum time for aspiration has not been duly considered It is well established that the number of organisms in tuberculous lesions increase greatly at the time of caseation and liquefaction Following removal of the abscess contents by spontaneous rupture, the organisms decrease rapidly so that their demonstration is difficult Second, an adequate enrichment and a light counterstain is absolutely necessary for maximum results

Undoubtedly many, perhaps most, of these abscesses rupture spontaneously before the surgeon is consulted, thus the best conditions for direct and immediate investigation have disappeared

It is evident that a method that can give a definite diagnosis within 2 hours after the specimen is received by the laboratory offers a distinct advance over former practice. In 1 of these cases a negative result by dilution-flotation led us to refrain from surgical procedure. The abscess healed spontaneously and 2 months later the guinea-pig confirmed the negative findings.

#### SUMMARY AND CONCLUSION

A comparison of the results obtained by dilution-flotation and guinea-pig inoculation in the demonstration of *Mycobacterium tuberculosis* in 18 anorectal abscesses is presented.

The two methods were in 100 per cent agreement in 13 abscesses aspirated by needle. Twelve were positive and 1 was negative by both. Under less favorable conditions in which the abscesses ruptured spontaneously with much loss of ma-

terial, they were in agreement in result in 3 of 5 abscesses investigated. Two were positive and 1 was negative by both. In the 2 other abscesses dilution-flotation was negative and inoculation was positive.

Dilution-flotation with picric acid counterstain offers a means for the immediate diagnosis of anorectal tuberculosis in the abscess stage, or its probable exclusion.

#### REFERENCES

1. BUTT, L. A., SMITH, N. D. and JACKMAN, R. J. The rôle of tuberculosis in anal fistula. *Surg. Gynec. & Obst.* 1930, 68-97.
2. JORRY, G. H. C. Ano-rectal tuberculosis. *Am. Rev. Tuberc.* 1930, 4-760.
3. PORTERMAN, J. E. The demonstration of *tubercle bacilli* in sputum. *Am. Rev. Tuberc.* 1931, 21-58.
4. Idem. Technique of sputum examination. *Am. Rev. Tuberc.* 1930, 407-58.





that particular branch of nursing. A nurse not possessed of such an aptitude and yet required to serve as a surgical nurse will suffer mentally because of her lack of experience and her ineptitude. In fact, she will be more of a hindrance than a help to the surgeon and indeed, in some immeasurable degree, may be responsible for increased morbidity or mortality percentages.

It is an accepted fact that a surgical operation is a serious undertaking and therefore anyone taking part in such an undertaking must be capable, well trained and experienced. If it is required that those who desire to become surgeons take special training to demonstrate their fitness to do surgery then similar standards of training and requirements should be established for the training of that very important part of the surgical team—the surgical nurse. Just as the prospective surgeon must take postgraduate training in surgery so should the nurse wishing to qualify as a surgical nurse be compelled to take postgraduate training in operating room technique. When, as part of their training, undergraduate nurses are assigned to the operating room, they should be under the supervision of trained and experienced operating table nurses and should work only as second nurses. In such a position they will not handicap the operating surgeon; they will be more calm and hence be better able to learn under the direction of one with sufficient experience and knowledge to teach them. Unfortunately it is true that the less experienced the surgeon the more apt he is to have to work with a relatively inexperienced and inept surgical nurse, despite the fact that he should be relieved of any confusion or lack of co-operation and should be free to concentrate exclusively on the operative procedure.

The time is not far distant when both that surgeon and that hospital will be out of step

with the times who do not include in operating teams an anesthetist who is qualified to employ all of the newer developments in the administration of anesthetics, an assistant who is at least in the process of being trained to carry out all of the major surgical procedures, and an operating nurse who has been specially trained for a relatively permanent position.

FRANK H. LANTY

## AN EVALUATION OF THE METHODS OF TREATMENT OF CRYPTORCHIDISM

THERE is a diversity of opinion among surgeons as to the best treatment for the undescended testis. Some believe that the ectopic gland is potentially malignant and should be removed. It should be said however that the undescended testis should not be considered a precancerous lesion as only about 3 per cent of such organs develop tumors (Human). Others believe that if left alone, most of these retained gonads will descend spontaneously. The reports of some investigators have indicated that the results from hormonal therapy are equally as good as, if not superior to those obtained by surgical treatment (orchidopexy). In formulating a rational plan of treatment of the undescended testis, one is influenced by the number and type of cases he has seen, his surgical experience and that of his associates, and the type of case that receives hormonal therapy.

It is an important question: What percentage of undescended testes descends spontaneously? If the majority of ectopic testes will eventually descend of their own accord as some investigators claim, the value of any kind of therapy is questionable.

There can be no doubt but that some aberrantly placed testes migrate to the scro-

tum of their own accord (Drake, Williams, Johnson) There is a difference in the reported incidence of ectopy before and after puberty According to Johnson, Williams and Drake, the incidence of cryptorchidism in younger boys is 17 to 42 per cent, in adult men gonadal ectopy occurs in 02 to 03 per cent This may mean that the hormonal changes incident to puberty produce descent in a large percentage of cases However, another explanation may be the inclusion in the prepubertal group of a number of testes of the migratory or retractile type (physiological ectopy, pseudocryptorchidism, or ectopy *en relour*) It is important to differentiate true (anatomical) from the pseudo or physiological type of cryptorchidism, as many cases of the latter descend spontaneously into the scrotum at puberty There is no convincing evidence that testes anatomically retained by mechanical obstructions to descent ever descend spontaneously Moreover, the finding of cryptorchidism in adult men is irrefutable evidence that all undescended testes do not descend spontaneously

The treatment of undescended testes by gonadotropic substances is generally recognized, but the results of treatment are varied Bigler, Hardy, and Scott and Nixon in their reviews of the early literature found that descent was said to occur in 60 to 75 per cent of cryptorchids treated with pituitary or pituitary-like extracts Later reports have been less enthusiastic The studies of Thompson and Heckel, Mumpress, and Rea showed descent in only 16 to 31 per cent of ectopic testes treated by endocrine therapy The dosage and length of treatment with anterior pituitary-like substances is quite varied in the cases reported in the literature Thompson and Heckel wonder if the percentage of patients showing descent spontaneously at puberty would be the same as that following the use of

anterior pituitary principle before puberty Thus, as a result of hormonal therapy, descent of the testis would be obtained only in those cases in which the testes would descend normally at puberty

It is impossible to give a final estimate of the value of gonadotropic substance in the treatment of ectopic testes For one thing, the incidence of spontaneous descent is not accurately known Furthermore, it must be ascertained whether endocrine therapy causes descent only of those testes which would descend without therapy about the time of puberty Hormonal therapy may make it possible to differentiate between those testes which require surgical interference because of mechanical obstruction to descent and those that do not

Treatment of the retained testis may be deferred until the patient is nine to eleven years old, since the testis does not grow grossly or microscopically until puberty, (Wangensteen) If one cannot be certain that the case is one of pseudocryptorchidism or true undescended testis, there is no great harm in waiting until after puberty before instituting treatment The practice of delaying treatment too long is to be condemned, however, knowing how atrophic the testis becomes when left in an aberrant position

A course of hormonal therapy should be given first to see if the additional hormonal stimulus will cause the gonad to descend into the scrotum If no results are obtained, an orchiopexy should be performed From the experience at the University of Minnesota Hospitals, it may be said that (a) spontaneous descent of a true undescended testis is a rare occurrence, (b) that the results following the use of gonadotropic substance in cryptorchidism have been disappointing, and (c) that the most satisfactory treatment of ectopic testis is orchiopexy

CHARLES E. REA



# TEXTS AND DOCUMENTS

## TO A MEDICAL GRADUATE UPON BEGINNING HIS HOSPITAL INTERNESHIP

**I**N the main corridor of the Cook County Hospital beside the elevators that carry a never ceasing stream of doctors, internes, nurses, visitors, is a bronze plaque inscribed in memory of Christian Fenger. The interested reader cannot but wonder, "What sort of man was this to merit such recognition?" and the thoughtful interne may ask himself, "Could I accomplish anything to merit such a tribute from my successors?"

The story of Christian Fenger, of his life and of his contributions to surgery, and particularly to Chicago surgery, has been told many times<sup>1</sup>—only recently in a beautiful tribute by Dr. James B. Herrick.<sup>2</sup> Everyone has dwelt particularly on his prolonged preparation for the practice of medicine, his indefatigable industry, his willingness to help young men. In Billings' words

"soon after his arrival in the country, he was persuaded by his countryman and friend, Dr. S. J. Jacobson, to locate in Chicago. Dr. Jacobson introduced Fenger to the members of the staff of the Cook County Hospital and he was invited to conduct a few autopsies at that institution. His scientific demonstration of pathological anatomy created such an impression that Dr. Isaac N. Danforth, who held the appointment of pathologist to Cook County Hospital, immediately tendered his resignation for the purpose of making the position available to Fenger. From the spring of 1878 until 1893, Fenger was the chief pathologist at the County Hospital, for 14 or 15 years the autopsy room at the County Hospital was the Mecca of medical students, internes, and members of the medical profession of Chicago who for the first time in the medical history of the Middle West had an opportunity to witness scientifically conducted autopsies and to learn the fundamentals of morbid anatomy and pathology.

"In 1879, Fenger served in the surgical wards for the various members of the surgical staff of the

hospital when they were absent from the city on vacations. This surgical service gave him the opportunity to introduce Listerism—antiseptic surgery—in the Middle West. In 1880 Fenger secured appointment with a regular surgical service in the County Hospital in which he continued for the next 12 years.

"From 1880 to 1884 he was curator of Rush Medical College Museum, in 1884 he was appointed professor of surgery in the College of Physicians and Surgeons, in 1893 he became professor of surgery in the Northwestern University Medical School, and in 1899 he became professor of surgery in Rush Medical College affiliated with the University of Chicago. He was surgeon in chief of the Passavant Memorial Hospital, the German Hospital of Chicago, and the Lutheran Tabitha Hospital from the time they were organized until his death. From 1893 to 1899 he was attending surgeon at the Mercy Hospital, Chicago, and from 1899 until his death, he was attending surgeon at the Presbyterian Hospital.

"he won success in practically every project undertaken. His knowledge of morbid anatomy and of pathology was phenomenal for that day and was attained by unremitting energy during his life in Denmark and Egypt and his earlier experience in the United States. This knowledge of pathology and of morbid anatomy made him one of the great surgeons of his time. He never became a brilliant operator, but what he lacked in operating skill was more than compensated for by thoroughness and knowledge of pathology. In diagnosis he was unsurpassed by any of his living contemporaries. He spoke five or more modern languages, but did not possess a ready command of any language. Nevertheless, he was a great teacher and though his speech was usually marked by halting words, he was able to impart knowledge to others with greater clearness than most teachers with fluent speech. He was especially fond of young men who showed by their every day lives that they had a thirst for knowledge and expressed this by purposeful, enduring work. He spent hours of his valuable time, both of the day and night, in the instruction of young medical

<sup>1</sup>Frank Billings, *Surg. Gynec. & Obst.* 1922, 35: 365-369.  
Alton Ochsner, *South M. J.* April 1938, 447-451.

<sup>2</sup>Proceedings of the Institute of Medicine of Chicago, 1941, 13: 318-319.

men in these interesting conferences he frequently forgot the passage of time in the apparent joy of teaching. It was through his influence that many of the young medical men of the period from 1880 to 1900 visited the clinics of Germany, Austria, France and England, and later became leaders in their chosen fields of work in the United States. While Fenger loved above every other thing in his professional life to help young men who were not afraid to work, he expressed an impatience with the frivolous and indolent men with whom he came in contact. Always he had the courage of his convictions and expressed them with blunt words which sometimes gave those unacquainted with him the idea of unfriendliness. But no man the writer has ever known was freer of envy or jealousy of others. Always he availed himself of every opportunity to express appreciation of the work of other men, provided it was characterized by honesty and efficiency. He was honest, intellectually and professionally. He was sincere and by nature simple in his deportment and daily life. He was free from cupidity and sympathetic with the poor, to each patient he applied all of the knowledge he possessed and all of the time necessary disregardful of financial reward.

Fenger lived in Chicago 24 years. During that period of time he exerted an influence in scientific medicine unequalled by any other individual. It was due to his influence and particularly as a pathologist that there developed such men as Nicholas Senn, John B. Murphy, William J. Mayo, Lewis L. McArthur and many others celebrated as great surgeons, and Ludvig Hektoen, E. R. LeCount, H. G. Wells, and others recognized as great pathologists, and many practitioners of internal medicine throughout the Middle West and in Chicago.

Christian Fenger passed from this life on March 7, 1902, but though 50 years have passed, he lives today in the hearts and minds of hundreds of physicians and surgeons who were proud to call him master, and he will continue to live through other generations by the work of his students and his pupils' students.

The rewards that came to Fenger were those that every doctor comes to prize above all others—the esteem, the affection, and the wholehearted admiration of his fellow practitioners.

Not long ago in a publication emanating from an interne group there appeared "Our Platform, and among other 'planks' the following:

Expansion of the educational program.

"Preferential consideration for our internes in making appointments for residencies.

"Financial remuneration for internes.

The contrast with the spirit and principles of action that motivated Christian Fenger's life struck me so forcibly that I was impelled to draw up a "platform" which seemed to me consistent with the spirit of a great institution. Perhaps I should call it "Resolutions Made on Beginning an Internship."

To be grateful for unlimited opportunity to expand my medical horizon in a relatively brief period of time and in unusually favorable surroundings. To appreciate the privilege and opportunity of following in the steps of Christian Fenger and Nicholas Senn or perhaps of Maurice Richardson, of Homans and Cabot or of Halsted and Oiler and Finney. To emulate their example and to prove a worthy successor to them.

To co-operate with everyone on my service so as to render the most efficient possible care to the patients entrusted to me. As a junior to be loyal, prompt, ready for any task that will help to "make things go." As a senior to direct and organize the work of the ward so that the younger men will secure the maximum of training and experience so that the medical students who come to the hospital as clerks will strive to secure a place on our service so that the nurses will feel it is an opportunity and privilege to help care for our patients.

To treat with special consideration the patients who come under my care knowing that many of them are the world's less fortunate children and that they are in the hospital, not because of their confidence in my ability to help them, but because they have nowhere else to go.

To be sympathetic and kind to relatives and friends, realizing that in the practice of medicine one must consider the family as well as the patient, and that unless I can gain and hold the confidence of both my efforts may be fruitless. To remember that the reaction of the responsible member of the family to a request for consent to postmortem examination of the baffling and unusual case that has not responded to treatment may depend entirely on the impression he has gained as to the degree and sincerity of my interest in the patients under my care.

To make an accurate record of the history and of the examination of each patient so

that the evidence may be complete and permanent To keep notes of important cases with names, dates, and diagnosis, so that I can recall them for reference when the occasion arises

To leave no stone unturned to make an exact and accurate diagnosis of every patient in my ward

To give every patient under my care the benefit of the best treatment that the hospital and modern medical science afford

To make a list each morning of the half dozen patients that require special care and attention for the next 24 hours if they are to recover from the serious illness they have contracted To explain the need for special care to the responsible nurses, so that their interest is quickened and their efforts directed with intelligence and effectiveness

To try to anticipate trouble and not to wait until catastrophe stares us in the face To provide a suitable donor and to be ready for blood transfusion before the patient is *in extremis*, to give the intravenous fluid before dehydration is obvious to the most casual observer To prepare my surgical cases properly for operation, to see that the necessary instruments and apparatus are available and in good order, to provide for the cast or splint or retention apparatus that may be needed after operation

To ask myself each evening before I leave the ward if there is something still undone that cannot wait until morning—some case of bleeding to check for evidence of recurrence, some splinted arm or leg to check for position or pressure of bandage or cast, some intravenous fluid to be given

To keep on my bedside table some journals and books, so that every evening before I turn off my light I can spend 20 minutes reading the *Journal of the American Medical Association*, *SURGERY, GYNECOLOGY AND OBSTETRICS*, the *Annals of Surgery*, or the life of Christian Fenger, of Robert Jones, of Osler—men after whom I would wish to pattern my life and conduct

To remember that if I “do today’s work today” I need not be concerned about tomorrow and next month and next year

“ in the summer of 1871, when I was attending the Montreal General Hospital, much worried as to the future, partly about the final examination, partly as to what I should do afterwards, I picked up a volume of Carlyle, and on the page I opened

there was the familiar sentence—‘Our main business is not to see what lies dimly at a distance, but to do what lies clearly at hand’ A commonplace sentiment enough, but it hit and struck and helped, and was the starting-point of a habit that has enabled me to utilize to the full the single talent entrusted to me

“The load of to-morrow, added to that of yesterday, carried to-day makes the strongest falter Shut off the future as tightly as the past No dreams, no visions, no delicious fantasies, no castles in the air, with which, as the old song so truly says, ‘hearts are broken, heads are turned’ To youth, we are told, belongs the future, but the wretched to-morrow that so plagues some of us has no certainty, except through to-day The day of a man’s salvation is now—the life of the present, of to-day, lived earnestly, intently, without a forward-looking thought, is the only insurance for the future Let the limit of your horizon be a twenty-four hour circle On the title page of one of the great books of science, the *Discours de la Methode of Descartes* (1637), is a vignette showing a man digging in a garden with his face towards the earth, on which rays of light are streaming from the heavens, above him is the legend ‘*Fac et Spera*’ ‘Tis a good attitude and a good motto Look heavenward, if you wish, but never to the horizon—that way danger lies Truth is not there, happiness is not there, certainty is not there, but the falsehoods, the frauds, the quackeries, the *ignes fatui* which have deceived each generation—all beckon from the horizon, and lure the men not content to look for the truth and happiness that tumble out at their feet Once while at College climb a mountain-top, and get a general outlook of the land, and make it the occasion perhaps of that careful examination of yourself, that inquisition which Descartes urges every man to hold once in a lifetime—not oftener

“Waste of energy, mental distress, nervous worries dog the steps of a man who is anxious about the future Shut close, then, the great fore and aft bulkheads, and prepare to cultivate the habit of a life of Day-Tight Compartments Do not be discouraged—like every other habit, the acquisition takes time, and the way is one you must find for yourselves I can only give general directions and encouragement, in the hope that while the green years are on your heads, you may have the courage to persist” (“A Way of Life” by William Osler An Address delivered to Yale Students)

It has often been said, “The world bows down to the man who works” It might be said with equal truth that the world is likely to pass with impatience, and perhaps a touch of scorn the man

who constantly stands with outstretched hand and plaintive voice saying "Gimme."

A beautiful tribute to Sir Robert Jones in the *Journal of Bone and Joint Surgery* in 1933 vol 15, pp. 541-543 begins and ends with the following paragraphs

"The kindly word, the cheering smile, the twinkling eye the whole magnetic personality of Sir Robert Jones remains only as a memory. The world's greatest orthopaedic surgeon has completed his life's work quietly as he was born seventy four years ago at Rhyl on the North Wales coast, just as quietly he died in the early days of this year at a little village in Montgomeryshire.

Throughout his career he practised in Liverpool and Liverpool has paid its last and greatest tribute to the honor of one of its citizens. The

ashes of Sir Robert Jones are the first to find a resting place within the walls of the Cathedral. The urn stands on a column of stone, close to the foundation pillar beneath the stained glass window dedicated to 'Service. As long as the walls of that vast cathedral stand, they will shelter all that has died of Robert Jones, as a token and memorial of his service to mankind. In the hearts and minds of those who came within the glow of his presence and who learned humbly to love him his spirit still lives.

It was the spirit of Service that inspired and motivated the lives of Fenger and Osler and Robert Jones and it is that spirit that will bring life's finest rewards to their successors who are just beginning their careers in the profession to which we are proud to be enrolled.

SUMNER L. KOCH

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## REVIEWS OF NEW BOOKS

A TREATISE on genito-urinary diseases is presented by Pelouze in *Office Urology*<sup>1</sup>. He emphasizes the medical aspects of a urologic office practice. The anatomy and physiology of the genito-urinary tract are briefly given as a background for the analysis of the disturbed physiology and pathological lesions.

In this volume a most competent, experienced authority exposes to the reader the secrets and difficulties encountered in a successful urologic practice. Necessities, such as adequate office floor space, cleanliness, and equipment for simple routine laboratory procedure are covered in detail.

The discussion of gonorrhea is priceless. In simple and plain language the diagnosis and the gentle art and science of its treatment are uniquely presented. Adequate reasons for routine office use of Gram's stains are given. The pitfalls in smear diagnosis are likewise emphasized. Gram positive cocci may be mixed with gram negative ones due to variation in size, dye intensities, mutation or fission forms. Uncertainties of identification of cocci by cultures are pointed out. Subculture from liquid medium to solid medium will invariably change the chain formation on smears to clusters. The author states he has reached a point "where he does not know a staphylococcus from a streptococcus in ordinary cultures". In the treatment of gonorrhea the value and shortcomings of sulfanilamide and its derivatives are brought up to date. The fact that many patients remain carriers following sulfanilamide therapy is forcibly brought to the reader's attention. A warning to include a culture for the gonococcus in the criteria of cure in all patients treated with sulfanilamide is added to spare many innocent victims the disease.

The recognition and management of specific and nonspecific prostatitis is most comprehensive. The physician must be thoroughly familiar with the normal to recognize and interpret the abnormal. Not all normal secretions come from normal prostate glands. Repeated examinations will show evidence of infection and not irritation of a normal gland. Seminal vesiculitis is deflated as a common focus or harbinger of infection. Seminal vesiculograms are rarely indicated.

Adequate drainage is given as the primary remedial measure affecting genito-urinary infections. The following points are neatly made: (1) All genito-urinary infections produce pus. (2) In the presence of pus good drainage is essential. (3) All things

equal—the better the drainage, the better is the response. (4) Chronicity is the result of poor drainage. (5) An organ has an inherent tendency to get well unless there is an effective feeder in some poorly draining contiguous organ.

The influence of the mind upon the urinary and sexual function is well presented. Frequency of urination and nocturia may be psychic in origin. Urinary retention may be functional. To search the mind as well as the urinary tract is a safe precaution. Psychogenic sensory symptoms are not imaginary any more than the pain of a true neuritis.

A comprehensive review of this textbook reveals a brief inclusion of all major urologic lesions, diagnostic procedures and treatment, medical, instrumental, and operative. One is strongly impressed with the inseparability of "office urology" and "hospital urology". This volume should prove most helpful and instructive to all who are interested in genito-urinary infections. LEANDER W. RIBA

THE concise and well written volume of 135 pages by Handfield-Jones entitled *Surgery of the Hand*<sup>2</sup> is an excellent contribution to the subject of hand surgery and emphasizes again how far-reaching and important have been the results of Kanavel's pioneer work on infections and injuries of the hand. In his preface the author acknowledges his indebtedness to Kanavel, and in discussing the subject of infection and injury constantly refers to his teachings. Two-thirds of the volume is devoted to a discussion of infections of the hand and their sequelae, a second section of 23 pages to injuries, and the final section of 21 pages to other surgical lesions.

In reviewing a volume which is so well written and which stresses wisely and forcefully correct surgical principles it may seem unduly critical to select anything for adverse comment and in doing so we would not detract from the commendation that has been expressed. In discussing prevention of infections after injury the author states (p. 7) "Should the hand be dirty more harm than good can be done by washing. The injured part is immersed in a bath of tincture of iodine for three minutes, the skin edges being separated to give access to the iodine." One would like to substitute for this advice the suggestion that simple soap and water cleansing followed by irrigation with sterile salt solution, if carried out within 2 hours of the time of injury, is an ideal method of transforming a contaminated wound into a clean surgical wound that can be re-

<sup>1</sup>OFFICE UROLOGY WITH A SECTION ON CYSTOSCOPY By P. S. Pelouze M.D. Philadelphia and London W. B. Saunders Co. 1940.

<sup>2</sup>SURGERY OF THE HAND By R. M. Handfield Jones M.C. M.S., F.R.C.S. Baltimore The Williams & Wilkins Co. 1940.



paired and closed with safety and with every likelihood of primary healing.

On page 60 on the anastomosis, I believe that immediate suture of ensheathed tendon is both feasible and dangerous whereas a free tendon should be tilted at once." Such advice seems to ignore the fact that the result of any tendon suture depends first of all upon securing primary wound healing and without infection. *Tendons should be sutured unless the surgeon is convinced that the wound is a clean surgical wound.* The fact that infection is likely to be more disastrous if it occurs with a tendon sheath does not affect the essential principle involved.

Throughout the volume excellent illustrations have been used which add greatly to its attractive appearance and to clarity of the discussion. Altogether this contribution is an excellent and desirable addition to the literature of surgery of the hand.

STANLEY L. KOCHE.

THE 10 volume set entitled *Abdominal Operations* by Malinow, containing some 300 pages, would seem to be more properly entitled "Surgical Conditions of the Abdomen" since at least as much space is devoted to discussion of the etiology pathology symptoms, and diagnosis as is given to the operations. There are many nicely executed drawings of operative procedures which help clarify the accompanying descriptions.

The first volume covers abdominal incisions, stomach and duodenum, spleen, pancreas, gall bladder and bile ducts. These subjects are fully discussed and many references are made to the current literature, though not always to the most recent contributions. A more critical stand by the author in handling the subject of suture materials and wound closure technique would be thought desirable by many surgeons. The operations of the stomach and duodenum are covered in considerable detail.

Volume 2 considers the liver, appendix, peritoneum, mesentery, omentum, external abdominal hernia, intestines, and postoperative chest conditions. The greatest allotment of space is given to the vermiform appendix in this volume. American contributions to colon surgery are prominently mentioned.

The impression is given of a rather thorough review of the literature by the author possibly not quite sufficiently critical to help the untrained surgeon and offering little new material for those well trained.

THOMAS C. DOUGLASS.

THE first four chapters of *Diseases of the Urethra and Penis* by McCrea are devoted to the anatomy anomalies and congenital malformations. The discussion of gonorrhea is brief. For its treat-

ment, four-foot Janet urethral grand lavages 1 cc daily and urethral instillations of 1 to 5 per cent protargol solution four times daily are recommended. Definitive value was assigned to the use of vaccines in acute Neisserian infections. The sulfonamide group is mentioned, but the author feels it is too early to say whether or not the results claimed are unduly optimistic. In a series of 2770 patients with gonococcal urethritis treated at St. Luke's Hospital, Manchester complicating epididymitis was noted in 53 patients, or 7.7 per cent. The treatment of acute epididymitis is given as either palliative or operative. A word on gonorrheal arthritis is included.

The subject of urethral strictures is well covered. Classification may be made according to their response to treatment. Surgical treatment of urethral strictures, including their resection, is illustrated in detail, and the treatment of pilafalls are emphasized. The discussion of penile and urethral tumors and foreign bodies is adequate. There are many interesting photographs and a few colored drawings.

This volume sums up the bibliography and opinions of many foreign writers on diseases of the penis and urethra, thereby lending itself as a handy reference on these subjects.

LEONARD W. RICE.

THE volume *L. Emmett Holt, Pioneer of Children's Century* is of distinct value in the different ways first and most important perhaps, as historical outline of the early history and growth of pediatrics as a medical specialty in this country, and second, as the biography of a late Victorian physician in New York City. The authors have produced a readable and interesting work from these points of view. Because the subject matter is not particularly dramatic, it would probably interest a limited number of people. However anyone interested in the history of medicine or in the medical life and manners of this period will enjoy reading it. I should imagine, however, that the sale of *The Care and Feeding of Children* will exceed and outlive its author's biography. A well tabulated index is included.

C. ANDERSON ALDRICH.

THE book *Hydrocephalus* by Marburg is curiously confusing. One can excuse sentences the structures of which are more German than English even such luxurious but lumpy terms as "hydrocephalus occlusus anterior of Guttman," "subependymal luxuriantia," and "transmineralization" can be managed by a patient reader. However one gains the impression that the opinions expressed in this book have been formulated more through a critique of the work of others than by personal experience and observation by the author. One feels that possibly the author has a completely clear under-

L. EMMETT HOLT, PIONEER OF CHILDREN'S CENTURY, by B. L. Duffin and L. Emmett Holt, Jr. Foreword by Edwards A. Park, M.D. New York, London & Appleton-Century Co. 1926.  
HYDROCEPHALUS, ITS ETIOLOGY, PATHOLOGY, PATHOPHYSIOLOGY, AND TREATMENT, by Otto Marburg, M.D. New York: Oskar Parey, 1926.

ABDOMINAL OPERATIONS. By Stanley Malinow, F.R.C.S. (Eng.) Vol. 1 and 2. New York and London: D. Appleton-Century Co. 1926.  
DISEASES OF THE URETHRA AND PENIS. By E. D'Arcy McCrea, M.D., M.Ch. (Dub.), F.R.C.S. (Ed.), F.R.C.S. (Eng.). Baltimore: The Williams & Wilkins Co. 1926.

# SURGERY

## GYNECOLOGY AND OBSTETRICS

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### SYNOVIAL SARCOMAS IN JOINTS, BURSAE, AND TENDON SHEATHS

A Clinical and Pathological Study of Sixteen Cases

DOMINIC A. DE SANTO, M.D., ROBERT TENNANT, M.D., and PAUL D. ROSAHN, M.D.,  
New York, New York

**C**LINICOPATHOLOGICAL knowledge of sarcomatous tumors in general has lagged somewhat behind similar knowledge of epithelial tumors. The former show such marked histological variability that classification is frequently an expression of individual opinion. While in many instances, the classification of sarcomas may seem to represent an academic nicety, nevertheless it is highly essential if one is to draw accurate statistical conclusions and avoid misinformation as to the efficacy of any form of treatment. Progress in the study of mesenchymal tumors, however, is surely being made, and the identification of a synovial sarcoma with specific synovial characteristics represents an achievement in this direction.

Synovial sarcoma would appear to be a rare disease if the reports in the literature are to be regarded as trustworthy. It is our feeling, however, that this rarity is far more apparent than real. Histological recognition of the tumor is often difficult unless certain specific features are demonstrable. Failure in

this regard will relegate the tumor to an improper category. Moreover, clinical recognition is difficult particularly as regards the intra-articular tumors involving the knee joint. Here the disease remains undiagnosed for from 5 to 6 years, and the patients are usually treated for chronic synovitis or for cartilage injuries.

There have been several excellent communications on synovial sarcomas, notably those of Sabrazes and his associates and those of Knox and of Berger. Wagner reported the first case in the American literature. This was studied by Ewing who called it a "fibro-endothelioma" of synovial origin. Coley's paper deals with the clinical features of the disease as they appeared at that time. The older literature is inadequate in that pathological descriptions are so incomplete and end-result studies so poor that conclusions are misleading. Mention should be made, however, of the papers of Stuer, and of Lejars and Rubens-Duval. The former described an "adenosarcoma" of the elbow region identical with our Cases 1 and 2, the latter described with excellent illustrations a similar tumor of the knee joint, and independently called attention to the fact that the tumor in some areas resembled an epithe-

From the Laboratories and Orthopedic Services of the Hospital for Ruptured and Crippled, New York; Department of Pathology, Yale University School of Medicine, and the New Britain General Hospital, New Britain, Connecticut.



*William Cumberland Cruikshank*

1748-1800

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lioma and in other areas a sarcoma. An "epitheliosarcomatous" histological appearance has thus become identified as a striking feature of most synovial sarcomas.

Smith writing in 1927 rediscovered these tumors and coined the designation synovioma to indicate their specific synovial nature and origin. This term unfortunately suggests a benign tumor. Mere synovial localization does not suffice to establish a tumor as a synovioma. Thus a hemangioma or chondroma of the synovial membrane is not a synovioma. The term "synovioma" has found such general acceptance however that it is difficult to displace. We are inclined to favor Berger's suggestion of synoviosarcoma or synovial sarcoma for the malignant tumors of specific synovial origin.

#### CLINICAL STUDY

The present study of 16 cases of synovial sarcoma was undertaken in a further attempt to study this obscure disease clinically and pathologically.

**Gross anatomy.** Synovial sarcomas originate in synovial tissue and thus are found in joints, para-articular bursae, and in tendon sheaths. In general they occur in or near a joint and since the relationships of the different synovial tissues are extremely variable and complex, it is often difficult in an individual case to establish the exact site of origin. This difficulty is enhanced when the tumor is of wide extent and of infiltrating character. Moreover the intra-articular synovial membrane is so frequently continuous with that of the para-articular bursae that bursal and intra-articular involvement may be simultaneous or successive.

Anatomically the tumors fall into 3 groups (1) encapsulated—Cases 1, 2, 3, 8, 9, 10 (2) circumscribed—Cases 4, 6, 12, 13, 14, 15, 16 (3) diffuse—Cases 5, 7, 11.

The majority of encapsulated tumors take origin from the synovial membrane of a para-articular bursa and the capsule is formed by the bursal wall. Circumscribed tumors may originate in a bursa or a tendon sheath. Diffuse tumors are classically seen within the knee and show simultaneous or successive involvement of joint, suprapatellar pouch, and

popliteal region. Indeed they may even invade the adjacent bones.

The gross appearance of the tumor is subject to considerable variation. It may be solid fibrous, and homogeneous, essentially like an encapsulated fibrosarcoma. In general however it appears soft, and myxomatous at least in areas. Grossly cystic areas and clefts are occasionally recognized. Yellow-brown pigmentation of the tumor with hemosiderin is sometimes observed, similar to that of the benign xanthomatous giant cell tumor (Cases 10, 13 and 14). Focal areas of calcification, chondrification and ossification are found more frequently than in other soft tissue sarcomas (Cases 1, 3, 6, 8, 9, 11). Broders encountered calcification in only 11 of 152 cases of soft tissue sarcoma, and Shields Warren, who reviewed 155 cases, did not mention it at all. Moreover it is not unlikely that among fibrosarcomas showing calcification and ossification there may not be some overlooked synovial sarcomas, since the pathological distinction is often impossible without prolonged study.

**Location.** The location of the tumor in our 16 cases, to which are added 21 authentic cases from the literature is shown in the table. Although the series is small it is impressive in that approximately half of these tumors occur in or about the knee joint.

| Site of lesion | Total number of cases | Location  |                |        |
|----------------|-----------------------|-----------|----------------|--------|
|                |                       | Articular | Para-articular |        |
|                |                       |           | Bursa          | Tendon |
| Knee           | 14                    |           |                |        |
| Elbow          |                       |           | 5              |        |
| Forearm        |                       |           |                |        |
| Shoulder       |                       |           |                |        |
| Foot           |                       |           |                |        |
| Thigh          |                       |           |                |        |
| not            |                       |           |                |        |
| Total          | 37                    | 14        | 18             | 5      |

#### ETIOLOGICAL FACTORS

The etiological factors to be considered are (1) The rôle of trauma (2) the influence of chronic bursitis or chronic synovitis (3) age incidence (4) sex incidence.

**Trauma** Trauma was mentioned in 4 cases, in all of which the knee joint or its adjacent bursae was involved. In 3 cases the trauma was severe and direct, whereas in 1, it was indirect. In 1 case careful history elicited the onset of symptoms prior to trauma. Twelve cases gave no history of trauma. It seems most likely that trauma occasionally initiated the onset of symptoms but by no means produced the tumor.

**Chronic bursitis or synovitis** The progression of an inflammatory hyperplasia into a neoplasm has often been recorded. One of our cases (Case 3) occurred in an olecranon bursa with a 10 year pre-operative history and strongly suggests that a previous bursitis may occasionally predispose to the development of a synovial sarcoma. The frequent localization of the knee tumors in the popliteal space where bursae are so prevalent, and the co-existence in both the benign bursa and the malignant tumors of blood pigment, bone, and cartilage, arouses further suspicion that, in rare instances, a chronic bursitis may predispose to the onset of a synovial sarcoma. The long duration of symptoms in the intra-articular knee joint cases also raises the query as to whether these were primarily, or became secondarily, malignant.

**Age at onset of symptoms** The age incidence is predominantly between the twentieth and fiftieth year with the average at 34 years. In Berger's composite series of 24 cases from which we have excluded 3 cases<sup>1</sup>, the average age was 35.4 years. The age incidence is notably younger than that for fascial sarcoma or fibrosarcoma of bone. In the former Broders finds an average of 43.2 years. In Warren's group of fibrosarcomas the average age is about 50 years. Smith, however, encountered an undoubted synovial sarcoma in a 7 year old girl. The tumor was located in the right knee and symptoms of internal derangement had been present for about 3 years.

**Sex** Synovial sarcoma occurs more frequently in the male sex—11 of our 16 cases and 13 of Berger's 21 cases. For the combined series the incidence is 24 males and 13 females. This differs but slightly from the sex

incidence of fascial sarcoma as reported by Broders and by Warren.

#### SYMPTOMS

Clinical symptoms of synovial sarcoma are neither striking nor characteristic. In xanthomatous giant cell tumor of joints and in hemangiomas of the knee joint, the symptoms are frequently of sufficient uniformity to permit of pre-operative diagnosis. An analysis indicates that (1) pain, (2) tumor, (3) joint dysfunction, (4) occasional fluid swelling of a joint comprise the chief clinical symptoms.

**Pain** Pain is not a constant feature being present only in 8 of our 16 cases. Here the duration of pain varied from 9 months to 10 years, and the patients were usually treated for synovitis. In all of the cases involving the knee joint, however, pain was present and the majority of these showed diffuse invasion of joint and para-articular structures. Some cases showed gross implication of a nerve trunk. Pain was absent or inconspicuous in the encapsulated or circumscribed para-articular tumors. Three of the painful cases involving the knee joint were explored and external semilunar cartilages were removed without the nature of the disease being discovered (Cases 2, 4, 11). Indeed, 1 case, Case 7, had two explorations without discovery of tumor. Many tumors were painless, localized, or encapsulated swellings as in Cases 1, 2, 3, 4, 9, 13.

**Tumor** Tumor was noted by the patient in 10 of 16 cases. The known duration of tumor varied from 1 month to 10 years with the average at 29 months. The location of the tumor undoubtedly influenced its discovery. Superficial tumors, as in the cubital fossa, olecranon, or wrist appeared early. Tumors concealed within the knee joint, popliteal space, or suprapatellar pouch eluded discovery for an average period of 5.6 years.

**Dysfunction** Dysfunction was present in 10 of 16 cases. It varied from slight restriction of motion to a severe painful flexion contracture, as illustrated in Case 4. Dysfunction was caused either by intra-articular involvement, or by pressure upon the joint structures by an adjacent tumor.

**Swelling** Fluid swelling occurred in only 2 of the 16 cases. Both cases (11 and 14)

<sup>1</sup> Berger's Case 4 was excluded because of incomplete data, his Case 9 is our Case 10 and Berger's Case 10 we re-examined and found to be a typical xanthomatous giant cell tumor.

showed intra-articular involvement. Centrifugation of the joint fluid and examination for tumor cells was unsuccessfully attempted. Fluid swelling which is quite common in joint xanthoma, would thus appear to be present only in intra-articular synovial sarcoma.

*Duration of symptoms* The average pre-operative duration of symptoms for the entire series was 36 months with extremes at 1 month and 10 years. The series is too small to permit correlation of the pre-operative duration of symptoms with end results. If those cases showing intra-articular knee involvement are considered separately however the pre-operative duration of symptoms was 5.6 years. Prolonged painful disability in a knee should always be regarded with suspicion.

#### ROENTGENOGRAPHIC EXAMINATION

X-ray examination was made in 13 cases and in 10 of these, a soft part tumor near a joint was visualized (Cases 1 6 8 9 10, 11 13 14 15, 16). In 4 cases (Cases 1 6 8 9) the tumor showed irregular calcification which facilitated x-ray visualization. In 3 cases (Cases 10 and 11) the tumor was overlooked on first examination but was readily discovered on review of the original films. One case (Case 5) showed increased intra-articular soft part thickening 5 years before the diagnosis of synovial sarcoma was established but this was not regarded with suspicion. Exception must be taken therefore to the statement that x ray films of synovial sarcoma are usually negative. Closer attention to soft tissue detail will undoubtedly lead to their more frequent discovery. Not unlike pneumarthrography will further improve x ray diagnosis. In Cases 5 and 8 extensive destruction of the bones comprising the knee was found without confirmatory x-ray evidence. A more comprehensive review of some of the roentgenographic features of synovial sarcoma are to be found in an article by Raymond Lewis.

#### TREATMENT AND END-RESULTS

The previous treatment accorded to synovial sarcoma has in our opinion erred by being too conservative. Treatment has generally consisted of local excision followed by delayed

amputation, unless the course of the disease was interrupted by widespread metastases. The frequent small size of the tumor its encapsulation and the long pre-operative duration of symptoms, all obscure the undoubted malignancy and lull the surgeon into an erroneous sense of security which is not warranted by the end-results.

*Treatment by local excision* In general, treatment of an accessible and resectable tumor by local excision results in prompt recurrence and essential widespread metastases. This statement is based upon an analysis of 13 cases which had undergone primary local excision (Cases 1 to 4 6 and 8 to 15). Of these 13 cases, recurrence was prompt in 10, in an average interval of 8.9 months, necessitating either secondary excision or amputation. One patient, Case 1 is believed to have developed axillary metastases, and 2 patients, Cases 2 and 9 seem well without disease but have been followed for only 14 and 9 months, respectively. One patient, Case 12 however is well 3 years after two excisions in spite of a prompt recurrence. Histologically it seems to be a less malignant variety of the tumor.

*Treatment by delayed amputation* In 7 cases (Cases 5 7 8 10 11 12 and 14) patients were treated by delayed amputation. This delay in amputation was usually the result of inability to arrive at a proper diagnosis. Five of these (Cases 8 10 11 12, and 14) had received one or more local excisions followed by prompt recurrence. Six of the 7 cases involved the knee joint and the seventh involved the flexor tendon of the ring finger. There are only 2 survivals of this group, Cases 12 and 14 for 22 months and 1 year respectively.

One conclusion that can be drawn from this small group of cases is that delay in amputation is not permissible in diffuse intra-articular synovial sarcoma.

*Value of x-ray therapy* It is virtually impossible at this time to evaluate the efficacy of x ray therapy. Ewing recently stated that in his experience synovial sarcomas responded rather favorably to intensive deep irradiation. In 8 of our cases (Cases 1 4, 8 10, 11 12, 15 16) patients received intensive deep x ray therapy after local excision. The tumor in

Case 1 has not recurred but patient has developed axillary metastases, in Cases 4, 8, 10, 11, 12, 15, and 16, lesions recurred promptly, Case 10, patient survived 10 years before dying of metastases, however Patients in Cases 8, 10, 11, 15, and 16 did not survive a 3 year period and in Case 4 a prompt local recurrence is scarcely compatible with a long survival

The final chapter in the proper treatment of synovial sarcomas will undoubtedly require revision We believe, however, that for the localized or encapsulated tumors, radical excision followed by intensive irradiation will permit time for pathological examination and gradation of the malignancy of the tumors Whereas all synovial sarcomas are malignant, there can be no doubt that the grade of malignancy follows the general rules for all malignant tumors We believe that the vast majority will require prompt amputation and that the decision as to amputation cannot be too long deferred Pathological distinction from the benign xanthomatous giant cell tumor is important to avoid needless sacrifice of an extremity It may be justifiable in occasional instances to allow time for a single recurrence, but it is never justifiable to await more than one recurrence The general practice of treating soft tissue sarcomas by repeated local excision has certainly not yielded brilliant therapeutic results Broders found from 7 to 45 per cent 5 year cures depending upon the degree of malignancy of the tumors and Warren reported 35 per cent 3 year cures Coley is convinced that the treatment of soft tissue sarcomas by repeated local excision results in more fatalities than would result if early amputation were more frequently resorted to Sabrazes would treat all synovial sarcomas by primary amputation

Treatment of diffuse synovial sarcomas, such as those which involve the knee joint, should be primarily radical at the outset Here the tumor usually involves joint, quadriceps pouch, and popliteal space, and attempts at local removal cannot fail to be inadequate Treatment may thus be summarized

1 Accessible tumors usually encapsulated should be treated by widespread local exci-

sion Pathological examination will permit gradation of the tumor and allow a short period of observation Amputation may be deferred to the time of the first recurrence but never beyond this

2 Inaccessible or unresectable tumors such as those of intra-articular localization should be treated by immediate primary amputation

3 X-ray therapy may retard the growth of some tumors and can be employed after local excisions

#### HISTOLOGY AND PHYSIOLOGY

Before undertaking a discussion of the histological features of synovial sarcoma it is well to review existent concepts concerning the structural and functional characteristics of normal synovial membrane

In a previous communication, Wilson and one of us reported 9 intra-articular xanthomatous giant cell tumors of synovial origin At this time the conclusion was formed that the tumor arose as a proliferation of synovial lining and subsurface cells in which the evolution of the tumor was frankly histiocytic The plasmodial giant cell, the large foam or xanthoma cell, the mononuclear cells with intracellular hemosiderin pigment, the so called "stroma" cells, and the lining surface cells were all regarded as modifications of a fundamental cell type or histiocyte At this time, the authors were unfamiliar with the histological studies of Francescini and the tissue culture experiments of Vaubel to whom priority is acknowledged for recognizing the histiocytic nature of the synovial membrane

Berger added additional histological evidence of the histiocytic nature of xanthomatous giant cell tumors by demonstrating an abundant delicate argyrophilic reticulum throughout their substance In cutaneous xanthomas which are more properly lipid histiocytomas, there exist, as Senear and Caro have shown, all transitions from a cellular histiocytic tumor without xanthoma cells but with abundant lipid demonstrable by sudan staining to an obvious xanthomatous tumor containing many foam cells We have also demonstrated an abundant arborescent argyrophilic reticulum in these tumors, which these authors did not point out



It seems quite apparent, therefore that in histological study the histocyte can at present be demonstrated in one or all of the following ways (1) demonstrable lipophagic properties, (2) demonstrable siderophagic properties (3) reticulin production.

In addition the histocyte possesses an endothelial appearance and tends to be polymorphous.

In the knee joint of the 4 month embryo we have observed a syncytial structure of the entire synovial mesenchyme manifested more prominently by a characteristic reticulum. Thus it may be stated that this histiocytic property of reticulin production in the synovial membrane becomes apparent at an early embryological age. Border cuboidal cells do not appear conspicuous and probably make their appearance at a later date. It cannot be assumed, however that the mere demonstration of reticulin is always synonymous with a histiocytic origin. In rhabdomyosarcoma, for example, reticulin production is sometimes as striking in our material as in so called reticulum cell sarcomas. There is great need for additional clarification of the complex problem of reticulin production in normal tissues and in connective tissue tumors.

Vauhel studied synovia by means of tissue cultures and pointed out peculiarities which distinguished it from ordinary mesenchyme. These were (1) a polymorphism of the cells in cultures with a tendency to produce round spindle, polygonal, and epithelioid cells and (2) a functional characteristic, namely the formation of synovial mucin. Berger reviewed the varying concepts concerning the true nature of the synovial membrane. He has regarded it as an histiocytic tissue related to the reticulo-endothelial system and capable of assuming different functional and histological appearances (1) a truly endothelial lining function played by the border cells, (2) a mucin-forming function, and (3) a histiocytic function—exhibited histologically by lipophagic and siderophagic properties, and by the production of a fine reticulin about the cells.

The classical experiments of Key and others demonstrated the phagocytic and migratory character of the synovial cellular constituents

when foreign materials were introduced into joint and further support the concept of the reticulo-endothelial nature of synovial membrane. In various forms of hemorrhagic synovitis, the siderophagic ability of both border and subsurface synovial cells is strikingly exhibited.

#### HISTOLOGY OF SYNOVIAL SARCOMA

All or any of the normal characteristics mentioned are variably exhibited in the sarcomas of synovial origin. Frequently these features co-exist as subsequent histological descriptions will show. In some cases the evolution of the tumor may be predominantly one sided and overshadow other characteristics. The histological appearance of fibrosarcomas and spindle cell sarcomas of fascial or perosteal origin is more characteristically uniform. Here, as Broders states a small area serves to identify and grade the tumor. For the identification of specific synovial characteristics, however multiple sections and careful differential staining are essential because the development of the tumor may be notoriously heterogeneous.

Endothelial characteristics exhibit themselves within the tumor characteristically as epithelioid gland-like spaces often enclosing mucin, or by reproduction of pavement-like areas of tissue strongly resembling epithelium or again, as neoplastic synovial villi. Where these characteristic features are strikingly developed, histiocytic features may be partly suppressed, although with reticulum staining one can generally identify two cell types in the tumor one, having the properties of a reticulum cell and another retaining endothelial or epithelial properties.

Mucin production may be confined to gland-like spaces or may appear as small interstitial accumulations among the endothelial components of the tumor cells. Grossly mucin production makes areas of tumor appear myxomatous or gelatinous.

Histiocytic properties may be exhibited in several ways:

1. The tumor may closely resemble a reticulum cell sarcoma and be composed of rounded oval, or reniform nuclei supported by a prominent argyrophilic reticulum. Here and

there one may find a gland-like space although this endothelial expression may be suppressed or limited to occasional microscopic areas

2 The tumor may be a polymorphous sarcoma with giant cells, irregular mononuclear, multinuclear cells, blood pigment again supported by a profuse argyrophilic reticulum, although such a tumor may superficially appear different from this description, it is essentially the same

3 The histiocytic evolution may take the form of sheets of xanthoma cells identical with those found in the benign xanthomatous giant cell tumor (see Case 4)

In general therefore all synovial sarcomas are reticulo-endothelial histiocytic sarcomas with varying degrees of reticulum production and endothelial evolution

Many areas of the tumor may show indifferent fibrosarcomatous characteristics, but careful study of multiple areas will reveal the tell-tale specific characteristics. For this reason any fibrosarcoma or spindle cell sarcoma located in or near a joint is very likely a synovial sarcoma, although proof of its identity must depend upon painstaking pathological investigation

For convenience, the appearance of the various histological expressions of synovial specificity in tumors are summarized in table, "malignant neoplasms"

#### MALIGNANT NEOPLASMS—SYNOVIAL SARCOMAS (SYNOVIOMAS)

- 1 Reticulo-endothelial characteristics (Cases 1, 2, 3, 4, etc)
  - a Composed of spindle cells (reticulum positive) and pale endothelial cells (reticulum negative)
 The endothelium may appear as
  - a A homogeneous pavement like structure with or without intercellular mucin
  - b Gland like spaces with or without mucin
  - c Papillary villi like structures (malignant synovial villi)
  - d Synovial borders resembling hyperplastic synovial membrane
- 2 Predominantly histiocytic features
  - a Polymorphous giant cell features, intracellular blood pigment (Cases 13 and 14 and areas of 10)
  - b May also contain cartilage (Cases 13 and 14)
  - c May reproduce synovial borders
- 3 Common fibrosarcoma or spindle cell sarcoma features may mask a true synovial sarcoma (Cases 6, areas of 10)

Our observations closely parallel and confirm those previously reported by Berger

However, we have been impressed with the extensive calcification, chondrification, and ossification which so frequently take place as scarcely to be coincidental. Calcification occurred in 6 of the 16 cases and had a predominate influence upon x-ray visualization. The calcium was deposited as small or large deposits in an afibrillar albuminoid interstitial substance not unlike that which forms the pre-ossseous substance of newly formed callus. Calcification was not related to x-ray therapy since it was discovered in each case before therapy was instituted. Two additional cases (Cases 12 and 13) showed large islands of fibrocartilage which led to the diagnosis of "chondromatous giant cell tumor"

Chondrification and ossification are less readily explained. In some instances it seemed to result from metaplasia. We suspect that it is closely related to the mucigenic tendency of synovial mesenchyme. Chemically, mucin is closely related to the ground substance of cartilage. Therefore, the detailed explanation of this complex tissue phenomenon must await further elaboration

#### MALIGNANCY OF SYNOVIAL SARCOMAS

All synovial sarcomas are malignant but in all probability all are not equally malignant. It would be premature at this time to attempt a histological grading similar to that of Broders for fascial sarcomas. Nevertheless, at the risk of being premature, one may hazard some expression of opinion as to the relative malignancy of the different forms

The least malignant tumors are those showing a high degree of histiocytic differentiation characterized by numerous multinucleated giant cells and pigmented cells, and fibrous areas. These tumors resemble somewhat the xanthomatous giant cell tumor or benign histiocytoma, although foam cells have been less conspicuous. Four of 16 tumors prominently exhibited these characteristics. Two patients showed prompt local recurrence. One such patient treated by two local excisions is well without disease after 3 years. One patient, however (Case 10), showed late metastasis and succumbed.

The most highly malignant forms are probably those tumors composed of numerous,

densely packed round, oval and reniform cells with abundant supporting reticulum. Experience indicates that these recur promptly and metastasize quite promptly to lungs, vertebrae, skull, and internal organs.

The tumors showing prominent endothelial characteristics with gland like spaces, appear to lie intermediate in their malignancy although all are undoubtedly capable of wide spread metastasis.

#### CASE REPORTS

**CASE** Synovialoma of right antecubital fossa. E. P. male aged 3 years. Treated by local excision and irradiation. Alive with villary metastases after 14 months.

A tin splitter aged 30, was admitted to the Englewood Hospital on May 2, 1939, for acute appendicitis. He also complained of difficulty in flexing and extending the right elbow joint for the past 6 months, and of a mass in the antecubital region.

Examination revealed that in addition to the signs of acute appendicitis, the patient presented a marked prominence of the anterior surface of the flexor group of muscles, overlying the anterior surface of the elbow joint. Extension was limited to 135 degrees, flexion to 90 degrees. Rotation was unimpaired. An x-ray film of the right elbow joint disclosed circumscribed soft tissue shadow extending to the humero-ulnar articulation with small foci of calcification. A pre-operative diagnosis of fibrosarcoma was made and on May 9, 1939, a local excision of the tumor was performed.

**Pathological report.** The specimen consisted of an encapsulated gray mass 4.5 by 3 centimeters with adherent synovial fringes. When sectioned the mass was found to be cystic and within the cyst were soft, gray papillomatous nodules, the largest about 1/4 centimeters in diameter undoubtedly the tumor originated from the synovial membrane either of the joint or from a synovial-lined bursa verifying the joint.

Microscopic sections prepared through the thickened area of the cyst all showed tumor which was highly cellular and exhibited many mitotic figures. There were two cell types in the tumor. One was an endothelial cell with oval, pale nucleus and an indistinct cytoplasm. These cells are arranged in rather compact masses and were supported by an amorphous pink-staining substance which in places was rather abundant and resembled secretion of mucin. The other type of cell was somewhat more elongated, with a darker staining nucleus and was arranged in anastomosing masses. In one area the tumor had a papillomatous appearance reproducing tufts resembling neoplastic villi. Here the surface cells assumed cuboidal character. Immunostaining revealed irregular pink-staining threads and strands which had the staining qualities of mucin. These seemed to be confined to the endothelial areas

of the tumor or about the neoplastic villi. With Laidlaw's reticulum stain the difference between the two cell types was greatly accentuated. Pale, non-staining areas corresponded to the endothelium like cells. The darker staining spindle cells are individually supported by a delicate reticulum. Other areas showed coarse deposits of calcium and true bone and about these areas the tumor assumed the character of collections of gland-like spaces composed of cuboidal cells. These were identical with areas from several other tumors.

Patient refused amputation and as given deep x-ray therapy to elbow and axilla. He was last seen in July, 1940, at which time discrete nodular masses were present in both axillae. Roentgenograms of the chest at this time were negative for metastases.

From a histological standpoint this case is a classical synovial sarcoma identical with Berger's Case 2. Small and large gland-like spaces, though not numerous, were present and papillary neoplastic villi predominated in other areas. Gland-like spaces also appeared lined by cuboidal cells and mucin was produced by the tumor.

Clinically the patient already has shown evidence of extension of the disease.

**CASE** Encapsulated synovialoma of right cubital region. Probable origin in bursa. Treated by local excision. Alive without evident disease after months.

J. B. aged 63 years. Ten years ago the patient noticed a small mass on the medial aspect of the right elbow joint. This gradually increased in size until 6 months ago when it began to enlarge more rapidly. On examination there was found a soft, almost cystic mass 3 centimeters in diameter at the medial aspect of the right elbow. There was no axillary adenopathy. On August 17, 1939, the tumor was removed by local excision. It did not communicate with the joint, tendon sheath.

The tumor was an encapsulated lobulated mass measuring 6 by 3.5 by 3 centimeters. The capsule as made up of strands of glistening tissue throughout which could be seen projecting gray and yellow nodules. It was soft in consistency and on section showed a homogeneous cut surface of glistening pinkish-white tissue in which whorls of dense tissue could be seen. When the cut surface was spread slightly slit-like spaces were seen between the bundles and whorls.

The tumor was enclosed in well defined fibrous capsule which in areas showed microscopic infiltration and replacement. It was composed of cells with pale endothelial nuclei and an indefinite cytoplasm drawn out into elongated spindle processes. The bulk of the collagen as intracellular but areas revealed moderate intercellular collagen. In many areas the collagen was more prominent, revealing itself as definite septa subdividing the tumor into rounded

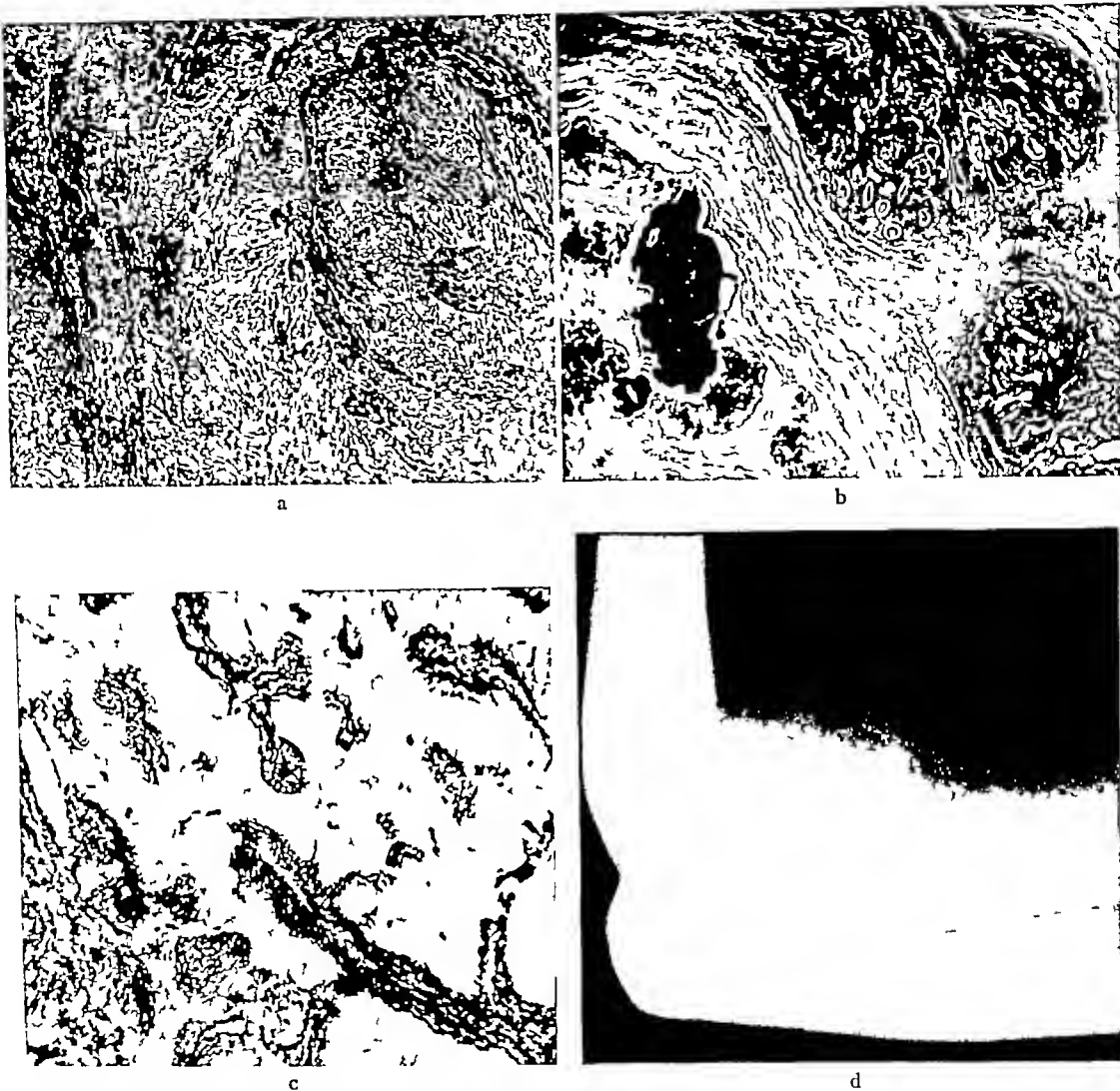


Fig. 1 Case 1 a, Photomicrograph showing general epitheliosarcomatous character of tumor. Note that there are two types of cells, darker staining reticulin positive and paler staining endothelial cells  $\times 80$  b, Photomicrograph of another area of tumor showing amorphous deposits of

calcium to the left and characteristic gland like spaces to the right  $\times 25$  c, Characteristic area of tumor, Laidlaw stain. The darker cellular elements are reticulin positive  $\times 90$  d, Roentgenogram of tumor showing focal calcification

nodules. In every microscopic field there were present great numbers of rounded, oval, and irregularly shaped gland-like spaces lined by cells which resembled cuboidal epithelium. On superficial examination one would be inclined to diagnose this an "adenosarcoma." The space formation exceeded that encountered in any of the 16 cases of the series. The transition between spindle and cuboidal cells in the tumor was extremely gradual. Other areas near the margin of the growth revealed predominately fibrosarcomatous characteristics, but even here there

were slit-like clefts in the tumor with spindle cells playing the border rôle. Reticulum stains were negative, however.

In July, 1940, eleven months after operation, patient was examined and found to be free of recurrence. There was no clinical evidence of pulmonary metastasis.

This case is histologically similar to Cases 1, 5, 7. It is the classical "adenosarcoma" of Stuer even in its location. Its origin was prob-



Fig. 2. Case 2. a, left. Cross section of tumor. b, Photomicrograph. The histological appearance is both "melesarcomatous" and fibrosarcomatous.  $\times 75$ .

ably in a para-articular bursa. Histologically it is composed of dedifferentiated fibrosarcoma like tumor and completely differentiated endothelium-like spaces. Intermediate reticulo-endothelial features appear lacking.

Clinically we believe recurrence or metastasis will undoubtedly occur unless the patient accepts further therapeutic measures.

**CASE 3.** Synovialoma of olecranon bursa: treatment by local excision.

C. V. female, aged 50 years, a housewife, was admitted to the second Surgical (Cornell) Division of Blevins Hospital, in November 1939, complaining of lump on her left elbow of 9 years duration. In the last 6 days, however, it had grown in size and had become red, inflamed, and tender.

Examination revealed over the posterolateral aspect of the left elbow a large mass 4 by 5 by 6 centimeters which was firm, red, inflamed, and slightly warm. The mass was fluctuant at its apex. Clinical diagnosis was inflamed olecranon bursa.

Patient was treated with wet dressings after which on November 20, 1939, through simple incision, the tumor was exposed and easily dissected free from the overlying skin. It was firmly attached to the underlying joint capsule and triceps fascia. The tumor was irregular firm, partially fluctuant, and extended over the radial head of the elbow joint.

When pathological study revealed that the tumor was a synovial sarcoma, patient was asked to return for amputation but refused. In May 1940, she returned with local recurrence at the operative site, which was re-excised.

The original tumor was ovoid in shape and measured  $\frac{1}{2}$  by  $\frac{1}{2}$  by  $\frac{1}{4}$  inches. The surface was

nodular and covered by a thin fibrous capsule. On section the tumor presented nodular fibrous consistency. In the center there was a cystic cavity about  $\frac{1}{4}$  inch in diameter.

Sections revealed a thin capsule of lamellated connective tissue which was rather vascular and which varied in thickness at different locations. Continuous with the capsule and filling the center of the tumor mass, was a rather dense cellular overgrowth composed of closely packed cells with nuclei that were rounded, oval, vesicular or reniform, and with prominent nucleoli. The nuclear membrane was sharp and distinct, the nucleus as pale the nucleolus was generally black, but sometimes had a faint pink tint giving it the appearance of an epithelial or endothelial cell. Mitotic figures were fairly numerous, 1 or 2 per high power field. In many locations, there could be seen two general cell types: fascicles of more elongated spindle-like cells and groups of more polygonal cells with rounded or oval nuclei. There were indefinite transitions between the two cell types.

In places the tumor was relatively acellular and the mass was subdivided by thick bands of calcified and ossified hyaline material which resembled fibrocartilage and connective tissue. There were also more delicate strands of pink staining material surrounded by closely approximated tumor cells which had the appearance of an albuminoid deposit within the tumor. In a rare instance it was possible to identify irregular endothelium like spaces within the tumor filled with a serous material and blood, and lined directly by cuboidal tumor cells. In a few areas the appearance was characteristic of fibrosarcoma with occasional large plasmoidal giant cells. Mucicarmine stain revealed slender positive threads of mucin among the cells. Kiehlum stain disclosed a uniform rich a basophilic reticulum surrounding individual and groups of cells.

The tumor is fundamentally a reticulo-sarcoma composed of rounded and elongated elements both of which are reticulum positive. Endothelial evolution is revealed by some well formed gland like spaces, but is less conspicuous than in Cases 1 and 2. Focal areas reveal fibrosarcomatous characteristics. Interstitial mucous production was prominent. Calcification and ossification were also observed.

Clinically without amputation the prognosis is unfavorable.

**CASE 4.** Synovialoma of right thigh probable origin in bursa overlying lesser trochanter: treated by local excision.

C. C., 26 year old colored house W, was admitted to the Meadowbrook Hospital on the service of Dr. Norman Treves, for tumor of the inner side of the right thigh, of 9 months duration. For the past 3 months, the mass had slowly increased in size and had caused occasional gnawing pain.

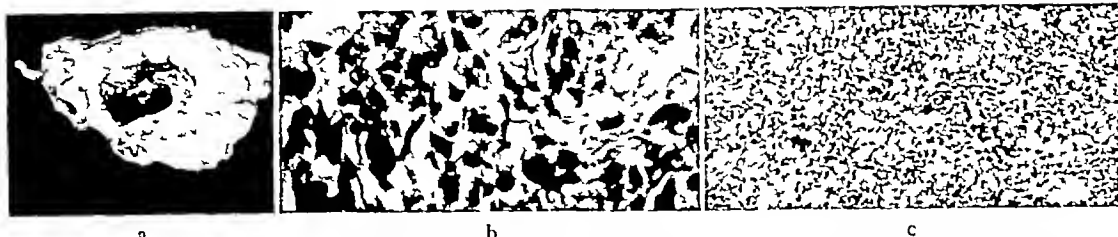


Fig 3 Case 3 a, Photograph of drawing of synovial sarcoma involving olecranon bursa,  $\frac{7}{12}$  actual size b, Photomicrograph showing characteristic reticulosarcomatous ap

pearance  $\times 235$  c, Photomicrograph, reticulosarcomatous area of tumor. Other areas show characteristic gland like spaces  $\times 60$

Examination revealed a firm, nontender, tumor mass about the size of an orange beneath the adductor muscles high up on the inner aspect of the thigh. A roentgenogram, January 19, 1940, showed a small mass on the upper end of the femur with a sharply outlined periphery of the same density as the muscle tissue. There was no evidence of bone involvement or of calcification.

A biopsy on January 23, 1940, resulted in a diagnosis of synovial sarcoma, and on February 17, 1940, a radical local excision of the tumor was performed. In spite of deep x-ray therapy the tumor recurred to its original size after a period of 3 months. Further data are not yet available, however, there is no doubt but that this case will terminate with generalized metastases.

Specimen was an encapsulated cystic tumor mass about 8 by 15 centimeters, which on section was friable and showed numerous xanthomatous areas which were revealed as yellow, circumscribed deposits throughout the tumor.

The microscopic features were quite similar to those in Case 1, with the addition that the histiocytic areas of the tumor could be shown undergoing evolution into large masses of xanthoma cells indistinguishable from those ordinarily found in benign xanthomatous giant cell tumor. In some areas the tumor was extremely fibrous and here the histologi-

cal picture was similar to that of benign xanthomatous giant cell tumor, with the additional finding of islands of endothelial cells which assumed a gland-like pattern. With the reticulum stains the distinction between the endothelial and histiocytic components of the tumor were more clearly demonstrated and the evolution of the reticulum elements into foam cells by a progressive lipophagic infiltration could be clearly shown.

Many areas showed a structure quite similar to that of a papillary adenocarcinoma, the papillary appearance reproducing synovial villi lined by cuboidal cells.

This case is most valuable from the histological viewpoint in that it demonstrates the widely varying cellular appearances that the tumor elements can assume. Dark-staining reticulum positive areas, pale endothelial areas, areas resembling papillary adenocarcinoma, and areas resembling benign xanthomatous giant cell tumor were all present. It also illustrates the fundamental histological identity of origin of the benign xanthomatous giant cell tumor which is essentially a benign histiocytoma and the malignant synovial sar-

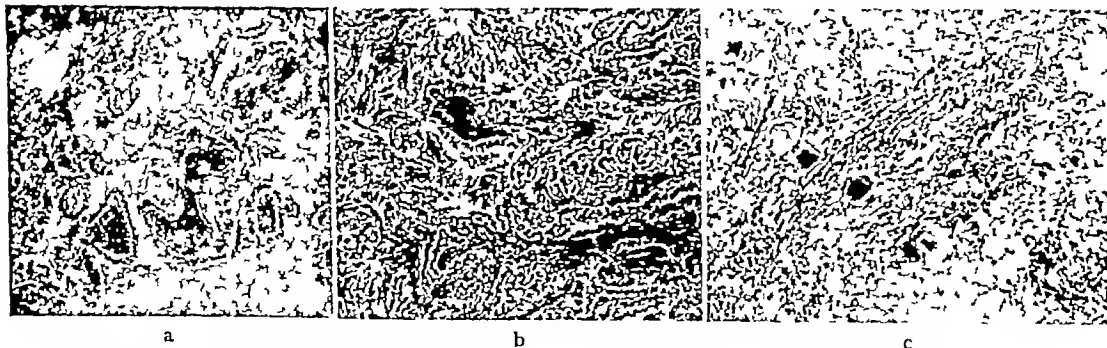
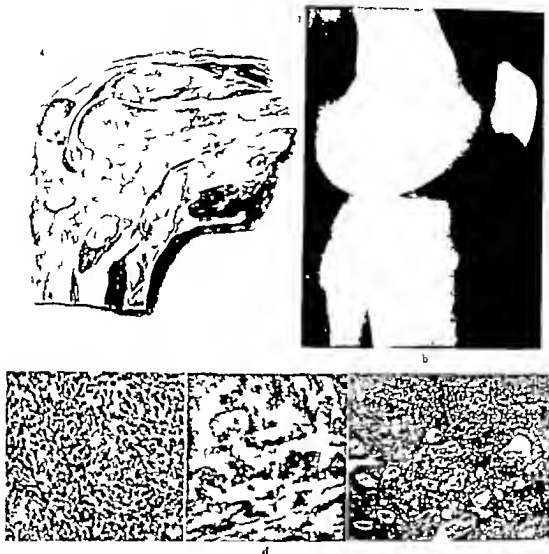


Fig 4 Case 4 a and b, Photomicrographs. Note the papillary character of the endothelial cells of the tumor reproducing neoplastic synovial villi. Note also the epithelioid sarcomatous character illustrated better in b and the xanthomatous transformation. The xanthomatous cells

may be traced to the darker staining reticulum positive elements of the tumor, confirming their histiocytic nature  $\times 75$  c, Another area of same tumor showing complete histiocytic differentiation scarcely distinguishable from that seen in benign xanthomatous giant cell tumor  $\times 63$



d

Fig. 5. Case 5. a, Photograph of drawing, preoperatively  $\frac{3}{4}$  actual size of specimen. b, Roentgenogram taken 5 years before amputation showing tumor in articular space, suprapatellar pouch, infrapatellar hyaline and popliteal space. Note that tumor has invaded the upper end of the tibia and the lower end of the femur. c, Photomicrograph of an area showing characteristic "adenosarcomatous" appearance. d, Similar area, Laidlaw stain.  $\times 75$ .

amputation showing increased intra-articular soft tissue. c, Indifferent area of tumor essentially reticulosarcomatous in character.  $\times 5$ . d, Similar area, Laidlaw stain.  $\times 75$ . e, Photomicrograph of an area showing characteristic "adenosarcomatous" appearance. f, h, the formation of gland-like spaces filled with mucin.  $\times 65$ .

coma which is essentially a malignant reticulo-endothelial sarcoma from synovial tissue.

**CASE 5.** Synovialoma of left knee joint and suprapatellar pouch and popliteal space. Terminating, 3 months after amputation, in generalized and pulmonary metastases.

**H. S.** 3 year old student, was first seen in the Hospital for Ruptured and Chipped, June 27, 1932,

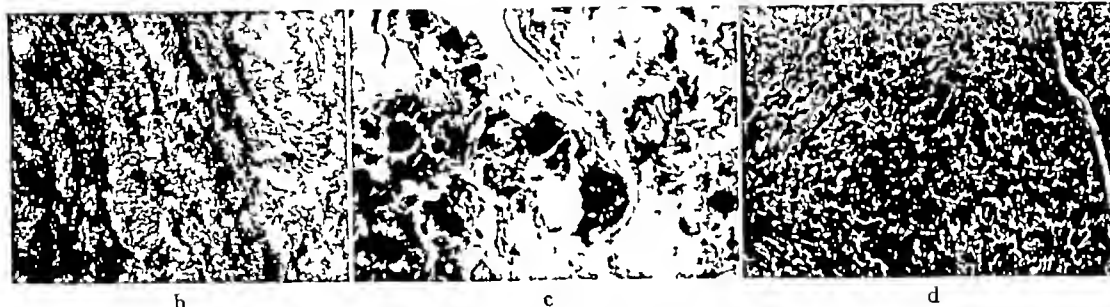
complaining of pain in the left knee for 8 months. Shortly before this onset he was hit in the left knee with hockey puck. Pain was aggravated by motion or exercise.

Examination of the tumor was essentially negative except for slight limitation of extension.

A roentgenogram, June 9, 1932, Dr. Raymond Lewis reported revealed "no bony changes and the joint spacing seems normal and symmetrical. There



a



b

c

d

Fig 6 Case 6 a, Roentgenogram of recurrent tumor showing focal calcification of soft part tumor b, Typical dedifferentiated fibrosarcomatous area of tumor  $\times 75$

c, Amorphous deposition of calcium Compare with Figures 1b, 8b, 9c  $\times 65$  d, Another area of tumor showing characteristic reticulosarcomatous evolution  $\times 65$

is a mottled increase in density of the soft tissues of the joint anteriorly below the patella"

A diagnosis of chronic traumatic synovitis was made and patient was treated by physiotherapy and strapping. He left the clinic, however, and consulted various physicians who treated him for arthritis. One year later he was operated upon at another hospital with a diagnosis of dislocated semilunar cartilage. This operation resulted in no improvement of the intense pain. In February, 1937, he presented himself with a large swollen left knee. Roentgenograms were inconclusive. The knee joint was explored and a tumor was encountered in the suprapatellar pouch. On February 9, 1937, an amputation at the junction of the upper and middle thirds of the thigh was performed for synovial sarcoma. Roentgenogram of chest at the time was negative for metastases. After amputation, patient was given 7 injections of Coley's toxin.

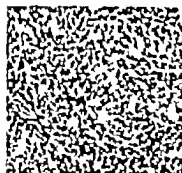
On May 25, 1937, a chest x ray film disclosed many metastases scattered through the lungs. He

gradually weakened and died on March 15, 1938.

A fusiform swelling involved the entire region of the knee for about 6 inches above and below the joint. On sagittal section of the amputated extremity there is found a soft area of new-growth which apparently has its origin in the synovial membrane of the knee joint in its posterior aspect, and which extends into the suprapatellar pouch anteriorly and posteriorly for about 2 inches, invading the soft tissues of the popliteal space. It also invades the upper end of the tibia and the lower end of the femur.

Microscopic sections show a tumor composed for the most part of large rounded and blunt spindle cells with pale oval vesicular and reniform nuclei. The cells suggest endothelium in their general appearance and arrangement. The tumor for the most part is diffuse and compact, but in places the arrangement is loose and the tumor reproduces gland-like, irregular spaces filled with mucoid fluid. Elsewhere the cells are slightly elongated and spindle shaped, suggesting spindle cell sarcoma. In a few places it





d

Fig 5. Case 5. a, Photograph of dis. leg., approximately  $\frac{1}{3}$  actual size of specimen. Tra-articular synovial sarcoma showing tumor in joint space, suprapatellar pouch, infrapatellar ligament and popliteal space. b, That tumor has invaded the upper end of the tibia and the lower end of the fibula. c, Roentgenogram taken 5 years before

amputation showing increased intra-articular soft tissue. d, Different area of tumor essentially reticulo-sarcomatous in character. e, Similar area, Lactin stain. f, Photomicrograph of an area showing characteristic "adenosarcomatous" appearance, with the formation of gland-like spaces filled with mucus. X65.

coma which is essentially a malignant reticulo-endothelial sarcoma from synovial tissue.

CASE 5. Synovium of left knee joint and suprapatellar pouch and popliteal space. Terminating, 3 months after amputation, in generalized and pulmonary metastases.

H. S., 35-year-old student, was first seen at the Hospital for Ruptured and Crippled, June 7, 1933,

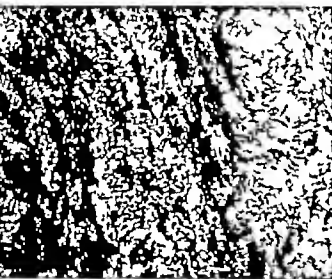
complaining of pain in the left knee for 3 months. Shortly before the onset he was hit in the left knee with a hockey puck. Pain was aggravated by motion or exercise.

Examination at that time essentially negative except for slight limitation of extension.

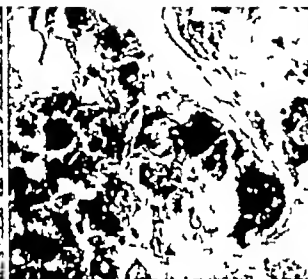
A roentgenogram, June 8, 1933, Dr. Raymond Lewis reported revealed "no bony changes and the joint spacing seems normal and symmetrical. There



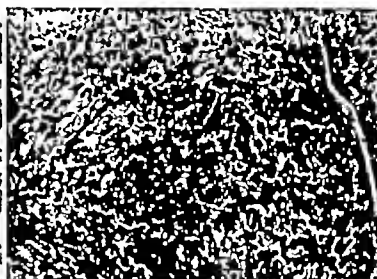
a



b



c



d

Fig 6 Case 6 a, Roentgenogram of recurrent tumor showing focal calcification of soft part tumor b, Typical dedifferentiated fibrosarcomatous area of tumor  $\times 75$

c, Amorphous deposition of calcium Compare with Figures 1b, 8b, 9c  $\times 65$  d, Another area of tumor showing characteristic reticulosarcomatous evolution  $\times 65$

as a mottled increase in density of the soft tissues of the joint anteriorly below the patella"

A diagnosis of chronic traumatic synovitis was made and patient was treated by physiotherapy and strapping. He left the clinic, however, and consulted various physicians who treated him for arthritis. One year later he was operated upon at another hospital with a diagnosis of dislocated semilunar cartilage. This operation resulted in no improvement of the intense pain. In February, 1937, he presented himself with a large swollen left knee. Roentgenograms were inconclusive. The knee joint was explored and a tumor was encountered in the suprapatellar pouch. On February 9, 1937, an amputation at the junction of the upper and middle thirds of the thigh was performed for synovial sarcoma. Roentgenogram of chest at the time was negative for metastases. After amputation, patient was given 7 injections of Coley's toxin.

On May 25, 1937, a chest x-ray film disclosed many metastases scattered through the lungs. He

gradually weakened and died on March 15, 1938.

A fusiform swelling involved the entire region of the knee for about 6 inches above and below the joint. On sagittal section of the amputated extremity there is found a soft area of new-growth which apparently has its origin in the synovial membrane of the knee joint in its posterior aspect, and which extends into the suprapatellar pouch anteriorly and posteriorly for about 2 inches, invading the soft tissues of the popliteal space. It also invades the upper end of the tibia and the lower end of the femur.

Microscopic sections show a tumor composed for the most part of large rounded and blunt spindle cells with pale oval vesicular and reniform nuclei. The cells suggest endothelium in their general appearance and arrangement. The tumor for the most part is diffuse and compact, but in places the arrangement is loose and the tumor reproduces gland-like, irregular spaces filled with mucoid fluid. Elsewhere the cells are slightly elongated and spindle shaped, suggesting spindle cell sarcoma. In a few places it

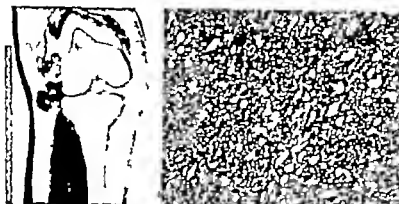


Fig. 7. Case 7 a, left, Photograph of coronal section of amputated specimen, somewhat reduced. Note that the internal semilunar cartilage has been removed. The bulk of the tumor is in close apposition to the joint. b, Photomicrograph of characteristic "adenomatous" area of tumor. X75.

is possible to trace the tumor to a lining synovial layer of cells. There are areas which show stream-like invasion of joint capsule and ligamentous structures. There is no tendency to reproduce cartilaginous or osteoid elements. A few large collections of typical xanthoma cells are also found. Sections of femoral condyle and upper tibia show replacement by similar areas of tumor. Mucicarmine stains fail to reveal the presence of mucin. With Laidlaw's reticulum stain two cell types can be distinguished. Clear negative areas correspond to the more rounded cells, and numerous positive fine threads of reticulum correspond to the more elongated cells.

Diagnosis: Synovial sarcoma (synovioma).

Histologically Case 5 is essentially similar to Cases 1, 2, 3, 4. The endotheliom-like areas are less numerous but are most typical and correspond to those in the classical descriptions of Stuer and of Lejars and Rubens Duval.

The pre-operative duration of symptoms in this case was 6 years. Pulmonary metastases appeared 3 months after amputation and death intervened 13 months after amputation. In spite of an exploration of the knee joint in 1933 the possibility of synovial sarcoma was not considered. The tumor showed bone invasion of great extent.

CASE 6: Synovioma of left lateral knee, probable origin in bursa of vastus lateralis. Treated by two local excisions. There has been no second recurrence after 3 years.

This patient G. B. was admitted to the Hospital for Ruptured and Crippled on August 26, 1938, complaining of painful mass on the left leg. It states that 3 years ago, while playing baseball, he was

"spilled" on the lateral aspect of his left knee with the shoe of another player. There was slight swelling and pain about the knee, and it was treated by hot applications until the symptoms disappeared. Three months later the pain and swelling recurred. These symptoms gradually increased during the next 8 months and at that time, 3 months after the injury, he consulted a physician. X-ray films were made and he was admitted to another hospital where tumor was excised, involving the semimembranous musculature and leading back to the popliteal space.

Pathological examination described a tumor measuring 5 by 3½ by ¾ centimeters, having the consistency of soft bone. On microscopic section, it showed incomplete ossification and calcification imbedded in hyalinized connective tissue. A few osteoblasts were scattered about the osteoid spicules. The final diagnosis was a benign osteoma.

Patient was free of pain for 3 months, after which it recurred, and gradually increased. The mass also recurred, growing slowly during the past year.

Examination revealed a well developed and nontender mass of 3 years. There was prominence on the lateral aspect of the left thigh immediately above the knee joint where a well defined tender tumor 7 by 7 centimeters could be felt. It was not attached to the skin but was attached to the deep structures.

X-ray films revealed a soft part tumor lateral to the knee joint, containing irregularly distributed lime. There was no evidence of primary bone or joint involvement. Chest plates were negative.

On September 16, 1938 the patient was again operated upon and tumor was exposed lying within the substance of the vastus lateralis muscle and apparently extending to the capsule of the knee joint. The tumor was excised, including much of the vastus lateralis muscle and some of the capsule.

The specimen was a flat, white, fibrous mass measuring 5 by 3 by 1½ inches with some adherent semimembranous muscle composing the edges. On sec-

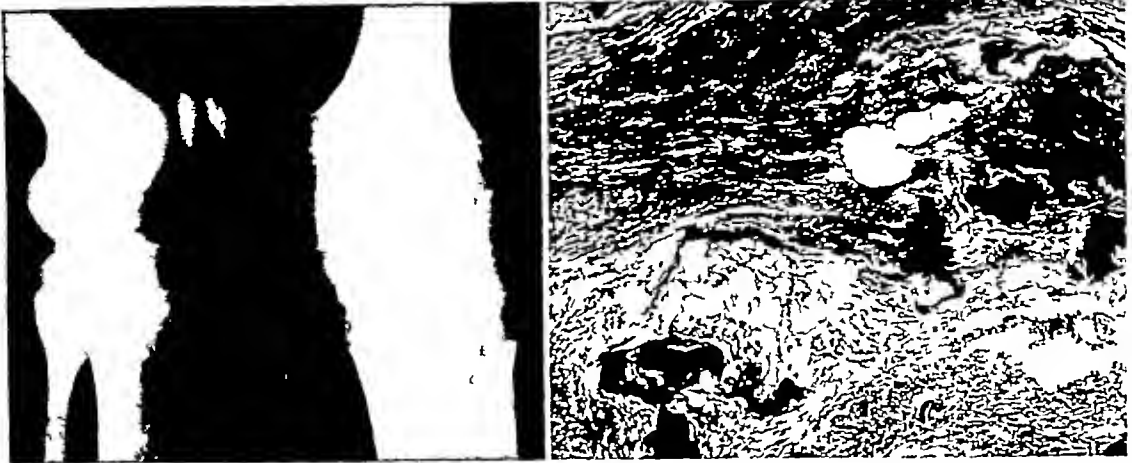


Fig 8 Case 8 a, left, Roentgenogram of recurrent calcified soft part tumor in popliteal space b, Photomicrograph of area of fibrosis and calcification. Synovial sar-

coma was not suspected until recurrence took place The recurrent tumor is histologically identical with that in Figure 5c.  $\times 78$

tion, it was found to be of tough fibrous consistence with some areas appearing soft and fish-like Other areas appeared bony hard in consistence

Large numbers of blocks of this tumor were studied in the attempt to establish the exact type of sarcoma In many areas the tumor presented the typical appearance of common fibrosarcoma, that is to say, it was composed of elongated spindle cells and elongated fibrils in a wavy fascicular arrangement In other areas, the tumor exhibited interstitial deposits of amorphous calcium present as small and large granules which could be seen undergoing various stages of chondrification and ossification About these areas there was a peculiar albuminoid impregnation of the stroma resembling somewhat the preosseous infiltration of osteoid tissue and identical in appearance with areas of Cases 1 and 9

Preparations of the soft fish-like areas showed a tumor of entirely different aspect Here the tumor was composed of a syncytium of cells with pale, oval nuclei with a definite nuclear rim and a prominent nucleolus In some areas the tumor elements could be seen grouped about small blood vessels In a few areas the arrangement of the cells was pseudoglandular and here they could be seen forming gland-like spaces This arrangement was definite, although it could be located only exceptionally

In these highly cellular areas, it was possible to trace the tumor to a definite synovial border, which resembled a hyperplastic rather than a neoplastic synovial membrane The cells along the border were flattened, but beneath the border there were fairly numerous, pale, oval nuclei which were difficult, if not impossible to distinguish from the endothelium-like tumor elements present in the deeper tissues Mucicarmine and reticulum stains of soft cellular areas showed anastomosing mucin threads and a rich fine arborescent reticulum around almost every cell

A diagnosis of synovial sarcoma was made and the patient was advised to have an amputation but refused

A report obtained October, 1939, indicates that the patient is working and apparently in good health It is our belief, however, that, without further treatment, dissemination of the disease is inevitable

The bulk of this tumor resembles a common fibrosarcoma of moderate malignancy (grade 1) Areas of calcification, albuminoid infiltration of the stroma lead to a suspicion of synovial sarcoma Soft areas of tumor sectioned revealed sheets of pale endothelium-like cells, synovial borders, and occasional gland-like spaces as well as intercellular threads of mucin The specificity of the tumor was thereby assured This case closely parallels one quoted by Berger as occurring in Sabrazes' laboratory in which (footnote p 534) the original tumor was identical with that in our Case 1 and Berger's Case 2, and the recurrence was indistinguishable from common fibrosarcoma Calcification and albuminoid impregnation, though not entirely specific features of synovial sarcoma, are helpful in arriving at the diagnosis Areas of reticulo-endothelial evolution although not so well developed as in Cases 1 and 2, are none the less strikingly dissimilar to the fibrosarcomatous areas

CASE 7 Synovioma involving right knee joint, popliteal space, and biceps femoris tendon, treated



Fig. 9. Case 9. a, Roentgenogram of tumor of dist. femur. b, Reticulosarcomatous area.  $\times 52$ . c, Another area showing calcification of tumor.  $\times 52$ .

for years as internal derangement of knee joint, later by amputation. Alive with pulmonary metastases after 23½ years.

E. S., a Jewish housewife aged 37 years, was referred to the New Haven Hospital on January 1, 1937. She first noticed pain in the knee in the summer of 1934 and in January 1935 after having wrenched her right knee in an automobile accident the pain had become worse. A diagnosis of rupture of the external semilunar cartilage was made and on January 30, 1935 the joint was explored and the internal semilunar cartilage was removed. In August 1935, she was readmitted to the hospital where she remained until September for correction of flexion contracture by a wedge cast. In January 1936 she was readmitted and a second arthrotoomy performed. A mass of necrotic granulation material was removed from the external posterior aspect of the cartilage and reported as follows:

Pathologically the specimen was received in several small pieces, the largest one measuring 5 by 5 by 1 centimeter. On section these pieces presented homogeneous cartilaginous structure. The microscopic sections showed cells of cartilage type. No evidence of any abnormal pathology could be found. The diagnosis as cartilaginous proliferation.

Röntgenographic examination of the joint in January 1935, was reported negative. Roentgenographic examination in December 1936 showed marked narrowing of the joint space, some moderate proliferation about the margin of the joint, and rather marked bone atrophy. Stereographic examination of the chest for metastases as indeterminate.

Physical examination revealed that "the patient's right knee was held at about 3 to 35 degrees flexion. Motion was extremely difficult to obtain. There was considerable peritarticular thickening. There were two operative scars, one over the lateral and anterior aspect of the joint centering on the joint line, and another overlying the lateral hamstring, above the lateral condyle. About the center of the scar crossing

the joint line there was a extremely sensitive nodule about 5 centimeters in diameter, present attached to the patella but so sensitive that it could not be satisfactorily palpated for mobility. There was a second movable nodule just above the head of the fibula apparently attached to the deep fascia. The third nodule was found medial to the external hamstring and firmly attached to the deep fascia. There were no enlarged inguinal lymph nodes.

A biopsy of one nodule was made and revealed the presence of sarcoma of synovial origin. On February 8, 1937, mid thigh amputation was performed. Examination of the amputated extremity showed a large tumor mass involving the knee joint and extending into the popliteal space. The patient has been followed since discharge from the hospital. In December 1936, she developed a cough and chest pains. Roentgenograms of the chest revealed extensive pulmonary metastases.

This case like the one reported by Hodgson showed a skin metastasis. The long history of joint disability suggests a primary origin in the joint synovial membrane with outward spread to popliteal space and biceps tendon. In spite of two explorations, the nature of the disease was not recognized. The degenerated tissue removed at second operation was probably necrotic tumor tissue unsuitable for recognition. Clinically the difficulty of diagnosis is similar to that encountered in Cases 2, 10 and 11. Histologically this case is identical with Case 5.

CASE 8. Synovoma of left knee joint and popliteal space symptoms of 6 years duration. Treated by local excision, deep X-ray therapy and delayed amputation. Death from pulmonary metastases 35 years after amputation.

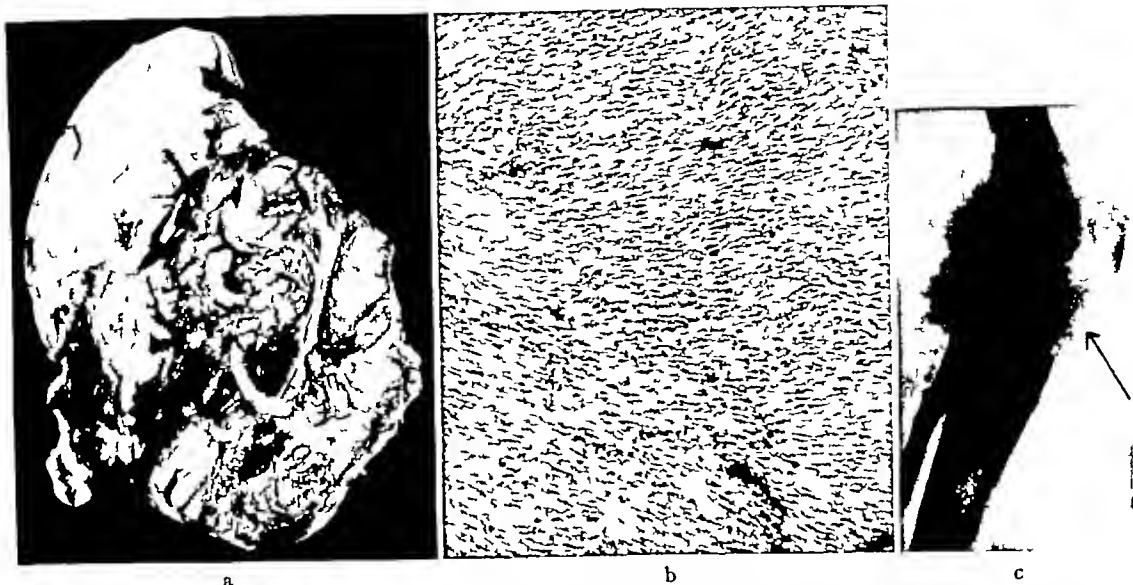


Fig 10 Case 10 a, Photograph of drawing,  $\frac{3}{4}$  actual size, large intra articular synovial sarcoma of knee joint. b, Photomicrograph of indifferent fibrosarcomatous ap-

pearance, dark areas represent hemosiderin pigmentation  $\times 100$  c, Roentgenogram showing large intra articular soft part tumor

L M, a student, aged 24 years, entered the Hospital for Ruptured and Crippled, October 16, 1935, complaining of pain and stiffness in his left knee of 6 years' duration. Six years ago, after falling down a flight of stairs, he injured the knee and following this, he had some swelling. A short time later he was kicked in the left knee and since then he has had pain and discomfort on the lateral aspect, which has grown steadily worse during the past 4 years.

Examination revealed a tender swelling over the lateral aspect of the knee joint. Flexion and extension were limited by about 15 degrees.

Roentgenograms showed a large irregular calcified body lying posterior to the lateral femoral condyle. This body dipped medially and forward into the intercondyloid notch. At the front of the joint opposite this projection there appeared a good sized oval body with an irregularly calcified periphery and a clear central area.

A clinical diagnosis was made of "calcified popliteal cyst," and on November 4, 1935, the mass was exposed through an incision over the outer side of the left knee. The outer portion of the gastrocnemius was cut and the popliteal space was exposed. From this area, the mass was found to extend forward into the posterior aspect of the knee joint.

The specimen was an encapsulated fibrous mass roughly ovoid in shape, measuring 3 by 2 by 2 inches. Adherent to the capsule there were some loose tags of fibrous tissue. On cross section it was found to be fibrous with nodular areas of cartilaginous and osseous consistence.

Microscopic examination at this time disclosed a fibrocellular tumor scattered throughout which there

were numerous amorphous deposits of calcium, many of which could be seen undergoing metaplasia into cartilage and bone. The stroma in places, was extremely hyaline and fibrous and throughout it were scattered pale oval nuclei which were interpreted as being chondroblasts because they were found lying in a medium resembling fibrocartilage. In addition, there was impregnation of the stroma by a hyaline albuminoid material which could not be positively identified, but which resembled pre-osseous infiltration of fibrous callus. Histologically, this was identical with that found in Cases 1 and 6. In some areas, the aspect was myxomatous being composed of a loose meshwork of stellate cells in delicate fibrils. In other areas, the aspect was fibrocellular, being composed of elongated spindle cells in a collagen-like stroma throughout which were scattered granules of intracellular and extracellular hemosiderin pigment. At that time the possibility of malignancy was not seriously entertained, and the mass was considered to be a calcified popliteal bursa.

Eleven months later, in October, 1936, he complained of a recurrence of his symptoms. Roentgenograms taken at this time revealed an oval soft tissue mass at the back of the joint, with some irregular, scattered, surrounding calcification. The mass seemed to be outside the joint.

Because of the recurrence, the original slides were reviewed. It was then thought that they represented some unusual form of synovial sarcoma. Patient was given deep x-ray therapy without improvement and after 6 months, amputation was advised.

Shortly thereafter he consulted a surgeon in Boston, who excised the recurrence which was found to

be frankly malignant and proposed amputation which the patient accepted.

Amputation of the left leg at the mid thigh was performed at the Massachusetts General Hospital, February 3, 1937. The pathological report is furnished by Dr. Tracy Mallory.

February 3, 1937

B 31 1434

Diagnoses Myxoiditis ossificans

Sarcoma type undetermined, (?) synoviomia.

**Femur Gross.** A left leg amputated at the mid thigh. The knee is markedly limited in motion owing to a large tumor mass of bony consistency which fills the popliteal space and extends over the lateral surface of the joint and the lower end of the femur. Overlying the tumor is a crescentic healed operative incision 6 centimeters in length. This lies approximately in the center of a circular area of erythema and tanning due to recent radiotherapy. After turning back skin flaps and careful dissection, a large tumor mass is finally dissected free. Though an apparent plane of cleavage between the tumor and the joint capsule is found, further investigation shows that the posterior portion of the joint capsule is diffusely infiltrated with tumor and measures 2 centimeters in thickness. The lower border of the tumor is fairly well delimited. It extends beyond the joint and thumb-like projection of soft tumor extends down almost to the head of the fibula. The upper margin is impossible to determine, the tumor infiltrating fibrosed atrophied muscles very widely. A fasciculus of muscle fibers about 1 centimeter in diameter extends upward within 5 centimeters of the line of amputation which is white partly fibrous, partly gelatinous, and contains granules of calcium. On section the central part of the tumor consists of cyst-like cells to 5 centimeters in diameter of calcified material, apparently bone, each of which encloses a central mass of poorly myxomatous tissue readily expressed by slight pressure. The peripheral parts of tumor show an intermixture of white fibrous tissue with the myxomatous material and only rare gritty granules. A occasional area shows frank fish-flesh character over an extent of 1 to 2 cubic centimeters.

**Microscopic.** The appearance of this tumor is as unusual as the gross. The tumor proper consists of infiltrating strands and masses of very uniform small cells with oval nuclei and scant neutrophilic cytoplasm which is occasionally drawn out into short spindle. There is tendency to fascicular grouping and also to bone formation. Practically no collagen is present between the tumor cells except in the immediate neighborhood of blood vessels and capillaries, and it is improbable that the tumor cells are producing the fibrils demonstrated with phosphotungstic acid hematoxylin. Despite the extreme cellularity, mitotic figures are astonishingly infrequent. The tumor is invading fibrous tissue and muscle bundles. Scattered irregularly through it are bony islands, occasionally with trabecular architecture. Many appear inactive but others are bordered

by osteoclasts and osteoblasts and show both lacunar resorption and also osteoid borders. The cartilage also both sharply circumscribed islands of inactive hyaline cartilage and no transitions from cartilage through mucinous tissue to ordinary fibrous tissue. No relation whatever between the bone and cartilage formation and the tumor cell can be made out. The appearances suggest an old focus of myxoiditis ossificans invaded by a new and entirely independent malignant tumor. The nature of this new malignant tumor is by no means clear. Neurogenic fibrosarcoma, endothelioma, and synoviomia are possibilities. In spite of the presence of epithelium like cells, the latter seems the most probable. It also offers the worst prognosis.

In February 1939, x-ray films showed definite pulmonary metastases. The patient died September 4, 1939, of pulmonary and generalized metastases. No autopsy was permitted.

Clinically the pre-operative duration of symptoms was 6 years. The interval from onset to death was 10 years. Death occurred 2 1/2 years after amputation and approximately 4 years after first local excision.

A comparison of the tumor with a previous case (Case 5), shows essentially the same round and spindle cell characteristics. Reticulum staining of the old blocks was unsatisfactory due to the age of the material. However, it was impossible to identify gland-like grouping of the cells. The identity with the previous case and other cases together with the localization and clinical course leave no doubt that this is a true example of synovial sarcoma. The calcification, chondrification, ossification and albuminous infiltration are identical with Cases 1 and 6. The histological identity of the tumor cells with that of Case 5 is further proof of the synovial origin of the tumor.

**CASE 9.** Synoviomia of left wrist region, treated by local excision. No recurrence within 9 months.

A. S., housewife, aged 34 years, complained of slowly progressive swelling of the anterior surface of the left wrist of 6 years duration. There was no history of pain or trauma.

Examination disclosed a swelling of the anterior and dorsal surfaces of the left wrist overlying the distal end of the radius and ulna.

An x-ray film on March 8, 1939, showed quite sharply defined rounded soft tissue tumor mass situated between the radius and ulna. This started just above the lower radio-ulnar articulation and extended up the forearm for a distance of about 4 centimeters. It bulged both anteriorly and posteriorly and it contained a rather irregular deposition of bone. There appeared to be a certain amount of pressure atrophy of the lower ulnar shaft.

X-ray diagnosis Probably synovioma

The patient was advised to enter the hospital for excision, but rejected this advice. She did, however, enter another hospital on March 30, 1930, where the tumor was excised.

The specimen consisted of a circumscribed tumor mass occupying a volume of about 4 centimeters in diameter. On section some areas of this tissue were found to be soft, and presented a homogeneous gray, waxy appearance. Other portions of the tissue contained small spicules of bone. In the main the tumor was composed of a homogeneous gray, waxy appearing tissue with occasional soft necrotic appearing areas.

One of the slides of the microscopic sections showed a densely cellular overgrowth of blunt spindle cells with somewhat rounded nuclei and poorly visible cytoplasm. The cells were compactly arranged somewhat in the manner of epithelial cells, and here and there one noted a mitotic figure among the nuclei. In places the arrangement was whorl like, elsewhere there were areas in which the cells were loosely arranged. In these areas the cells were frequently vacuolated and presented a pseudomyxomatous appearance. In addition, there was a tendency to form slit like spaces with an endothelial lining, and finally, in other areas the structure was highly fibrous, the cells assuming an elongated spindle appearance which resembled that seen in fibrosarcoma. Here the stroma was abundant, and the cells were not numerous, and there was considerable calcium deposition—the calcium appearing as coarse fragments. One small area shows actual bone formation. In general, the tumor exhibited a varied histological appearance and ranged in its appearance from a fibrosarcoma to areas which resembled a reticulum cell sarcoma.

Examination and x-ray film of the wrist in November, 1939, showed no recurrence of the disease.

**CASE 10** Synovioma of right knee joint. Treated by repeated local excision, deep x-ray therapy, and delayed amputation. Death 10 years after amputation, of pulmonary metastases. This case was reported in detail by Dr. Lewis C. Wagner and represents the first synovial sarcoma to be reported in the American literature. Follow-up data not then available are now furnished.

**H. N.**, a 35 year old musician, with an irrelevant family and past history, without any apparent cause, began to complain about 10 years ago of pain in the right knee. It was treated with the usual rheumatic treatment by the family physician but with no improvement. In the summer of 1923 he consulted a surgeon and the limb was immobilized in plaster without relief. The patient entered the hospital in October, 1923. Examination showed him to be in good health but he was walking with a slight limp, although the functions of the right knee were not impaired. There was a slight fullness under the right patella tendon. He brought a report of x-ray findings, which were normal. The case was thought to be one of chronic synovitis, and was treated conservatively with cautery and strapping. He did not

improve but, rather, the pain became worse. In January, 1924, an x-ray picture was taken, which showed a mass behind the patella tendon that was thought to be hypertrophied synovial tissue. A definite tumor was not considered but on looking back, it was easily recognized. On February 13, 1924, the patella was split and the knee joint exposed. A solid tumor covered by a synovial veil lay in the knee joint. It was attached to the outer antero-inferior border of the capsule by a small attachment. The tumor measured 7 by 5 by 3 centimeters, was elliptical in shape, and surrounded by a definite capsule.

The patient was free from pain for 1 year when the tumor reappeared on the lateral surface of the knee. An extensive resection of the capsule of the joint was done and the patient was again free from symptoms after the second operation. He received extensive x-ray therapy and a thorough course of Coley's toxin. In 1926 the symptoms and signs reappeared. The tumor had invaded the upper end of the tibia, under the patella tendon. Resection was unsatisfactory at the third operation and 2 weeks later a mid thigh amputation was done.

Examination March, 1930, showed the patient well and free from recurrences or metastases. In 1936, the patient succumbed from pulmonary metastases.

Through the courtesy of Dr. Francis Carter Wood, we were permitted to re-examine a slide which for the most part resembled a common fibrosarcoma. This tumor represents a dedifferentiated synovioma showing predominant fibrosarcomatous characteristics. On the authority of Drs. Ewing and Wood who examined many sections removed at the time of operation, it is included as an undoubted synovioma. Many areas show coarse clusters of intracellular hemosiderin pigment. Multiple sections and special stains could not be employed because the operative material was no longer available.

**CASE 11** Synovioma of left knee joint and suprapatellar pouch, treated by two local excisions and delayed amputation. Death from pulmonary metastases.

**R. L.**, a white Hebrew male, aged 25 years, was first seen in the New Haven Hospital in July, 1935, when he complained of pain and swelling in his left knee which he said developed following a baseball game. The patient had a history extending 6 or 8 years prior to this admission, when he noted that flexing the knee resulted in pain which could be eased by extending the leg. In the summer of 1934 the knee suddenly became swollen. No definite diagnosis was made and physiotherapy was instituted without improvement.

Throughout the summer of 1935 the patient continued to suffer pain and swelling. On this admission, roentgenograms were taken but no definite diagnosis was made. Upon review of these original films a definite suprapatellar tumor could be seen. After several days in the hospital the swelling gradually subsided and he was discharged to the ortho-



be frankly malignant and proposed amputation, which the patient accepted.

Amputation of the left leg at the mid thigh was performed at the Massachusetts General Hospital, February 3, 1937. The pathological report is furnished by Dr. Tracy Mallory.

February 13, 1937.

B M 1434

Diagnosis: Myositis ossificans.

Sarcoma, type undetermined (?) synovial.

"Femur Gross. A left leg amputated at the mid thigh. The knee is markedly limited in motion owing to a large tumor mass of bony consistency which fills the popliteal space and extends over the lateral surface of the joint and the lower end of the femur. Overlying the tumor is a crescentic healed operative incision 6 centimeters in length. This lies superficially in the center of a circular area of erythema and tanning due to recent radiotherapy. After turning back skin flaps and careful dissection, large tumor mass is finally directed free. Though an apparent plane of cleavage between the tumor and the joint capsule is found, further investigation shows that the posterior portion of the joint capsule is diffusely infiltrated with tumor and measures centimeter thickness. The lower border of the tumor is fairly well delimited. It extends beyond the joint and a thumb-like projection of soft tumor extends down almost to the head of the fibula. The proper margin is impossible to determine; the tumor infiltrating fibrous trochanteric muscles very widely. A fasciculus of muscle fibers about centimeter in diameter extends upward to within 3 centimeters of the line of amputation which is white, partly fibrous, partly gelatinous, and contains granules of calcium. On section the central part of the tumor consists of cyst-like cells at 2.5 centimeters in diameter of calcified material, apparently bone, each of which encloses central mass of poorly myxomatous tissue readily expressed by slight pressure. The peripheral parts of tumor show an intermixture of white fibrous tissue with the myxomatous material and only rare, gritty granules. An occasional area shows a frank fish-flesh character over extent of 1.5 cubic centimeters.

Microscopic. The appearance of this tumor is as unusual as the gross. The tumor proper consists of infiltrating strands and masses of very uniform small cells with oval nuclei and a scant neutrophilic cytoplasm which is occasionally drawn out into short spindle. There is a tendency to fascicular grouping and also to whorl formation. Practically no collagen is present between the tumor cells except in the immediate neighborhood of blood vessels and capillaries, and it is improbable that the tumor cells are producing it. No fibrils are demonstrated with phosphotungstic acid hematoxylin. Despite the extreme cellularity, mitotic figures are astonishingly infrequent. The tumor is invading fibrous tissue and muscle bundles. Scattered irregularly throughout are bony islands, occasionally with a trabecular architecture. Many appear inactive but others are bordered

by osteoclasts and osteoblasts and show both active resorption and active osteoid borders. The cartilage shows both sharply circumscribed islands of isotropic hyaline cartilage and no transitions from cartilage through mucinous tissue to ordinary fibrous tissue. No relation whatever between the bone and cartilage formation and the tumor cells can be made out. The appearances suggest a old focus of myositis ossificans invaded by a new and entirely independent malignant tumor. The nature of this new malignant tumor is by no means clear. Neurogenic fibrosarcoma, endothelioma, and synovialoma are possibilities. In spite of the absence of epithelium-like cells, the latter seems the most probable. It also offers the best prognosis.

In February 1939, x-ray films showed definite pulmonary metastases. The patient died September 4, 1939, of pulmonary and generalized metastases. No autopsy was permitted.

Clinically the pre-operative duration of symptoms was 6 years. The interval from onset to death was 10 years. Death occurred 3½ years after amputation and approximately 4 years after first local excision.

A comparison of the tumor with a previous case, Case 5, shows essentially the same round and spindle cell characteristics. Reticulum staining of the old blocks was unsatisfactory due to the age of the material. However it was impossible to identify gland-like grouping of the cells. The identity with the previous case and other cases together with the localization and clinical course leave no doubt that this is a true example of synovial sarcoma. The calcification, chondrification, ossification, and albuminoid infiltration are identical with Cases 1 and 6. The histological identity of the tumor cells with that of Case 5 is further proof of the synovial origin of the tumor.

Case 2. Synovialoma of left wrist region, treated by local excision. No recurrence within 9 months.

A. S., housewife, aged 34 years, complained of slowly progressive swelling of the anterior surface of the left wrist of 6 years duration. There was no history of pain or trauma.

Examination disclosed swelling of the anterior and dorsal surfaces of the left wrist overlying the distal end of the radius and ulna.

An x-ray film on March 8, 1939, showed quite sharply defined rounded soft tissue tumor mass situated between the radius and ulna. This started just above the lower radio-ulnar articulation and extended up the forearm for distance of about 4 centimeters. It belted both anteriorly and posteriorly and it contained rather irregular deposition of lime. There appeared to be certain amount of pressure atrophy of the lower ulnar shaft.

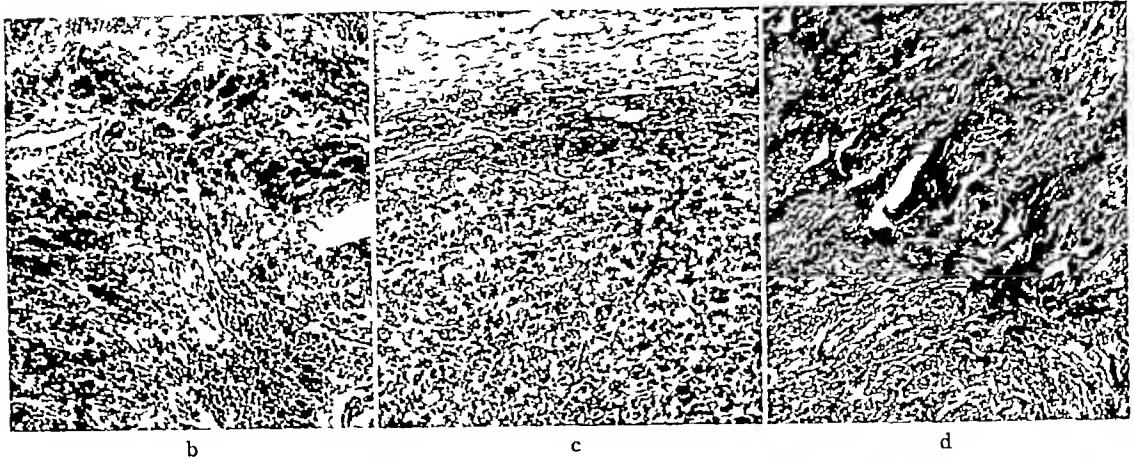


Fig 11 Case 11 b, Photomicrograph of a representative area of tumor showing histiocytic evolution, not unlike benign tumors of tendon sheath origin  $\times 68$  c, A metas-

tasis of the tumor in a popliteal lymph node  $\times 68$  d, An area of recurrent tumor illustrating its dedifferentiated fibrosarcomatous character  $\times 68$  Consult Figure 6b

several layers deep in a somewhat palisading fashion. Several popliteal lymph nodes are replaced almost entirely by tumor tissue. Here the tumor has an epithelial character. Strands and masses of small polyhedral and spindle (almost column-shaped) cells are arranged in a delicate connective tissue stroma. Again slit-like spaces lined by several layers of these cells are occasionally seen and in some places there is a suggestive papillary arrangement of the cells. The tumor in this specimen appears less well differentiated than in the first two, but still maintains the characteristic features. The rate of proliferation is also enhanced as indicated by the increased numbers of mitoses.

Clinically, this case illustrates the long preoperative course of the intra-articular synovial sarcomas. Pathologically many areas resembled the "giant cell" tumors of the tendon sheath type similar to that in Cases 12 and 13. A number of pathologists reviewed the slides on this case and regarded it as a benign giant cell tumor. On the basis of areas exhibiting reticulo-endothelial characteristics similar to that of previous cases it was regarded as malignant.

**CASE 12** Synovioma of superficial flexor tendon of fourth right finger treated by local excision, deep x-ray therapy, and delayed amputation.

E. S., a 32 year old housewife, noticed, in August, 1937, that the ring finger of her right hand was becoming stiff. This gradually progressed until it became painful to move the finger. About the middle of September, 1937, she noticed a slight swelling over this tendon which slowly increased in size. In October, 1937, she consulted a physician, who diagnosed an early Dupuytren's contracture, and pre-

scribed short wave diathermy. In February, 1938, the small tumor was excised and submitted for histological examination. The histological diagnosis was "synovioma." Since that time she has received 22 x-ray and 2 radium treatments.

On examination, the ring finger of the right hand showed an x-ray dermatitis with some sloughing and ulceration. There was little function of the finger and an ulceration over the palmar aspect of the right ring finger at the region of the proximal metacarpophalangeal joint.

Examination of the first tumor showed that it was composed of polyhedral and polygonal cells bearing a striking resemblance to epithelium. The cells were present in compact masses which were generally enclosed in delicate trabeculae of connective tissue. The nuclei were pale, oval, or vesicular. The nucleolus was prominent. Mitotic figures were not observed. In other areas the tumor cells appeared elongated, spindle in character, and assumed the character of tumor fibroblasts. The cytoplasmic boundary was distinct and the cytoplasm was pale, sometimes vacuolated, sometimes translucent. There was no resemblance to xanthoma and giant cell tumor. Some areas resembled the tumor reported by Black, but it was impossible to use differential staining methods in the study of this tumor.

Amputation of the right hand and middle third of the right forearm was performed by Dr. Bradley L. Coley on May 10, 1938.

The specimen was a right hand and forearm amputated through the distal third of the forearm. On the palmar surface between the fourth and fifth fingers, there was an irregular ulceration about 2 millimeters in depth. On sagittal section through this area there was found an irregular zone of white tissue resembling tumor tissue, which implicated the tendons and extended down to the metacarpal joint of the fourth finger.



Fig. Case 17. a, Original roentgenogram showing tumor in suprapatellar pouch, overlooked at time of first examination.

pedic dispensary. The diagnosis at that time was considered to be traumatic arthritis with possible ruptured medial meniscus. Finally in March, 1936, he was advised to come into the hospital for operation.

Physical examination of the left knee revealed a slight fluid swelling of the joint. In the suprapatellar region a hard freely movable mass about 5 centimeters in diameter could be palpated. There was no limitation of motion except on flexion, and this was painful to 90 degrees. Some atrophy of the left thigh was evident.

On March 23 a tumor of the left quadriceps pouch was excised.

The patient was discharged April 7 1936 on crutches. On July 30, 1937 a roentgenogram of the knee revealed recurrent tumor of the quadriceps pouch. The patient was seen subsequently in Baltimore where he was reoperated upon in October 1937. At that time tumor tissue was removed from the suprapatellar and popliteal regions.

The patient subsequently returned to New Haven with several draining sinuses and with evidences of recurrent tumor. A course of deep ray therapy delivered through three ports, medial, lateral, and posterior about the left knee with 1800 roentgen units through each port, was given without improvement. In February 1938, an amputation of the leg was performed.

The patient died at home on December 7 1938, of pulmonary and generalized metastases.

The specimen removed March 23 1936, is a diamond shaped mass of firm pink gray tissue which measures 7 by 5 by 2.5 centimeters. The external surface is irregular except on one side where it appeared smooth and shiny. The cut surface is composed of whorls of dense gray hit tissue.

Microscopic sections show the mass to be composed of hyalinized connective tissue stroma embedded in which, in a haphazard fashion, are masses and strands of typical cells. These vary from spindle to polyhedral in shape and have ill defined cell outlines. The predominant cell is polyhedral in shape with small amount of pink staining cytoplasm and vesicular nuclei. Moderate numbers of these cells are in mitotic division. In many places the cells are arranged about slit-like lumina with layer of these cells lining the lumina. In other places the cells are arranged in spaces lined by flattened endothelial cells which appear to be blood vessels. Scattered throughout the section in many of the masses of cells are occasional multinucleated giant cells. One edge of this section has smooth, undulating synovial border which is lined by flattened layer of cells. Subjacent to this surface are masses of polyhedrally shaped tumor cells. This apparently represents the region of the tumor in contact with the suprapatellar pouch.

Histological sections of the recurrent tumor removed from the knee joint in October, 1937 showed structure similar to that of the original tumor.

The specimen removed February 1938, is the amputated leg which has previously been dissected at another hospital. The soft tissue has been removed from the bony framework. In the area over the patella, there are two longitudinal healed scars and in the popliteal space there is another scar which is incompletely healed. In its central portion a sinus communicates with the joint space. The articular surfaces of the joint are almost completely destroyed and have dull, granular, mottled yellow and red appearance. In the popliteal space are few somewhat irregular but fairly discrete nodules of mottled gray yellow tumor tissue. Some of these appear to be lymph nodes which are invaded by tumor.

Microscopic section through the sinus tract shows the surface covered by exudate of polymorphous clear leucocytes beneath which there is mass of granulation tissue infiltrated with lymphocytes, large mononuclear phagocytes, plasma cells, and polymorphonuclear leucocytes. The articular surfaces of the joint are destroyed and involved by this inflammatory process which extends into the underlying bone. There is no tumor in the joint but adjacent to the sinus tract are several nodules of tumor which infiltrate the connective tissue. The tumor is made up of spindle and polyhedral cells which are arranged in masses and strands throughout connective tissue stroma. The cells are variable in size and are basophilic staining. Numerous cells are in mitosis. Only occasionally do masses of these cells line up about slit like spaces where they are arranged

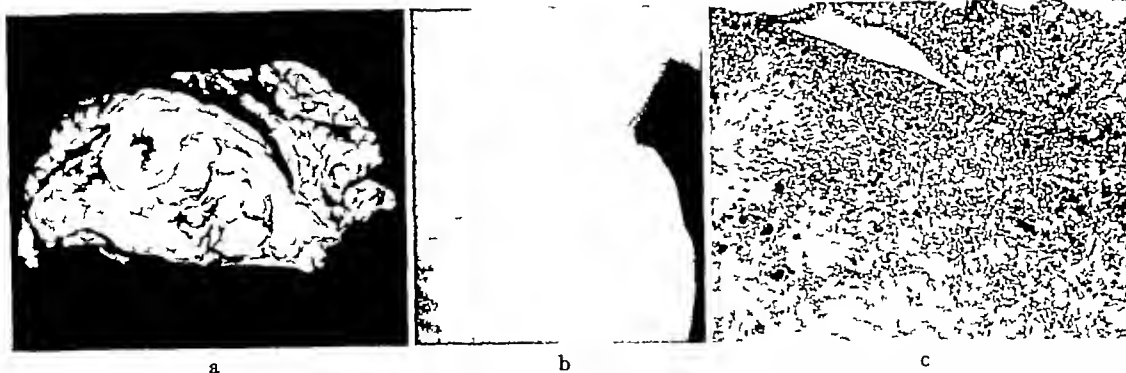


Fig 13 Case 13 a, Photograph of drawing of specimen,  $\frac{1}{2}$  actual size. Note the clefts and the areas of pigmentation. b, Roentgenogram of original tumor in popliteal space. c, Photomicrograph of a representative area of tumor illustrating synovial border. The evolution of the tumor is histiocytic and essentially similar to that shown in Figures 10b and 11b. Note the multinucleated giant cells and the coarse deposits of hemosiderin to the right.  $\times 65$ .

and posterior aspects of the left popliteal space, about  $3\frac{1}{2}$  by  $1\frac{1}{2}$  inches.

Through a vertical curved incision with the convexity toward the inner side, a tumor was exposed deep in the popliteal space. It was adherent to overlying muscles and tendons, and firmly adherent to the capsule. In removing the tumor it was necessary to remove a portion of the posterior capsule.

**Pathological report.** The tumor is circumscribed but does not have a distinct capsule. It measures 5 by 5 by 2 centimeters. Some loose tags of fibrous tissue are attached to the surface. On section the tumor cuts with a fibrous consistence and shows one fairly large cystic area about 1 centimeter in diameter. Scattered over the cut surface are firm, yellow, ground concentric nodules which have the consistence of cartilage. The intervening stroma is tinted in various shades from yellow to brown, the pigmentation being similar to that seen in xanthomatous giant cell tumor.

Because of the previous diagnosis of xanthomatous giant cell tumor, this tumor was studied by multiple section through a great many areas. The periphery of the tumor appeared largely encapsulated although the capsule was not complete. On superficial examination, there was found a striking dissemination of multiple deposits of intracellular hemosiderin pigment similar to that seen in xanthoma. Vast areas of the tumor presented a fibrocellular aspect, the cells being rounded, oval, blunt spindle, and irregularly shaped with oval and reniform nuclei. The arrangement of the cells was syncytial and this was better demonstrated by reticulum stains which showed both a fine and a coarse arborescent reticulum supporting the majority of the cells. In many of the areas, the stroma cells could be seen differentiating into multinucleated giant cells containing from 2 to 20 nuclei. In some fields giant cells were particularly numerous. Mitotic figures were fairly numerous about two per high power field. In many areas corresponding to the macroscopic concentric nodules, the stroma could be seen differenti-

ating into fibrocartilage. With both hematoxylin and eosin and Sudan III stains, it was not possible to demonstrate lipid in the tumor. Along one edge of the tumor was a well defined synovial border probably that of the semimembranosus tendon. This border showed reduplication of the synovial border cells and multiplication of the subsurface cells with areas of blood pigment similar to hemorrhagic villous synovitis as described in the knee joint.

Throughout the main tumor mass were numerous synovial spaces lined by from one to three rows of polygonal and flattened cells, and these spaces contain a metachromatic mucoid substance.

This tumor represents a form of synovial sarcoma histologically closely related to the xanthomatous giant cell tumor. It has been referred to as the "tendon sheath" type. It differs from xanthomatous giant cell tumor in the presence of typical synovial spaces, the presence of circumscribed areas of fibrocartilage, and the rarity or absence of demonstrable xanthoma cells in the recurrence. No exception is taken, however, to the report of xanthoma cells being present in the original tumor. While the presence of foam cells is a striking feature of xanthomatous tumors histiocytic tumors are frequently found with little or no demonstrable lipid. Berger in his Case 5 has reported what he regards as the first example of a malignant transformation of a xanthoma giant cell tumor in a white man 50 years of age, located in the anterior aspect of left thigh. This is identical with Berger's Case 5 showing synovial borders filled with blood pigment, classical giant cell features, and in original tumor, xanthoma cells.



Fig. 2a

Fig. 2. Case 2. a, Recurrent synovial sarcoma of fourth flexor tendon. Skin ulceration produced by intensive irradiation therapy. b, Photomicrograph showing histiocytic evolution of tumor similar to that in Figure 2b.  $\times 40$ .

In the slide of the recurrence there was considerable modification of the tumor probably as the result of the intensive irradiation. Here the tumor was sparse in loose fibrous stroma and was composed of syncytium of markedly degenerated spindle and irregularly shaped cells with indistinct cytoplasmic borders. In many areas where the nuclei were better preserved they had the same pale oval epithelioid-like aspect encountered in the primary tumor. Elsewhere they were shrunken and irregular. Here the tumor was robbed of its specific synovial characteristics. It could be traced, however, into the substance of the flexor tendon establishing its point of origin. Section through the base of the underlying metacarpal bone shows no evidence of infiltration by tumor.

In December 1939, patient had no evidence of generalization and was free of symptoms of disease. Chest roentgenograms at this time were negative.

Black's tumor was apparently benign although there was only a 10 month period of follow-up which seems inadequate to assure the benignity of the tumor. We regarded this tumor as malignant. Black subsequently reported a synovoma of the great toe and added additional follow up information of his first case occurring in the finger indicating that the course after 2½ years was still that of a benign tumor. It may well be that small synovomas in the tendons of the finger may run a more favorable course than the larger tumors about the larger articulations.

CASE 3 Synovoma of left popliteal space, probable origin in semimembranous tendon sheath, treated by two local excisions well 2 years later.

H. B. male, aged 43 years, was admitted to another hospital, on July 3, 1937, with history of a mass in the left popliteal space and slight stiffness of the knee joint for 6 months.

Examination of the knee revealed a hard, round mass about 2 by 3 inches located just below and in



Fig. 2b

the lower third of the left popliteal space. The mass was fixed to the deep tissues, but not to the skin.

X-ray film of the left knee in the anteroposterior and lateral views showed a circumscribed tumor approximately the size of an egg, in the popliteal fossa. There was no destruction of adjacent bones.

On July 3, 1937, through a transverse incision over the most prominent part of the mass, a firm circumscribed tumor was dissected out of the popliteal space. Sharp dissection was required to free it from the tendon sheaths and from the posterior capsule of the knee joint.

Pathological report August 2, 1937. The tumor, from left popliteal space, was a pinkish-gray ovoid mass 6 by 4 by 5 centimeters in diameter with firm small tags of fat adherent to the surfaces. It tags and two or three almond-shaped bodies which looked something like lymph nodes were adherent to the surface.

Histological examination showed that the stroma of the specimen consisted, for the most part, of polygonal and spindle cells with large numbers of large multinucleated giant cells. Moderate numbers of tumor cells revealed the presence of hemosiderin pigment in the cytoplasm. Some of the tumor cells were large and contained lipid substance.

Diagnosis: Giant cell sarcoma of tendon sheath (xanthomatous epulis).

Patient made an excellent postoperative recovery and was discharged on August 6, 1937. He was readmitted to the hospital on November 1937, with recurrence of the tumor.

Examination revealed a well-healed scar beneath which there was a firm, rounded mass in the medial

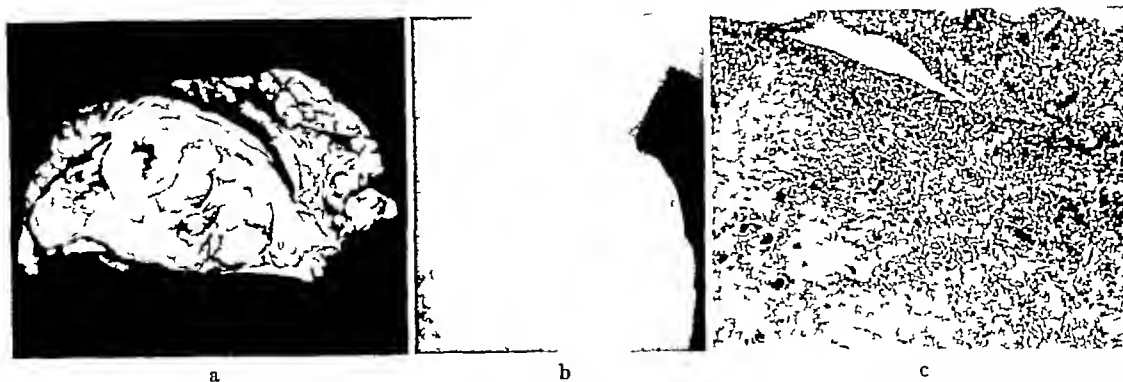


Fig 13 Case 13 a, Photograph of drawing of specimen,  $\frac{1}{2}$  actual size. Note the clefts and the areas of pigmentation. b, Roentgenogram of original tumor in popliteal space. c, Photomicrograph of a representative area of tu-

mor illustrating synovial border. The evolution of the tumor is histiocytic and essentially similar to that shown in Figures 10b and 11b. Note the multinucleated giant cells and the coarse deposits of hemosiderin to the right.  $\times 65$

and posterior aspects of the left popliteal space, about  $3\frac{1}{2}$  by  $1\frac{1}{2}$  inches

Through a vertical curved incision with the convexity toward the inner side, a tumor was exposed deep in the popliteal space. It was adherent to overlying muscles and tendons, and firmly adherent to the capsule. In removing the tumor it was necessary to remove a portion of the posterior capsule.

**Pathological report** The tumor is circumscribed but does not have a distinct capsule. It measures 5 by 5 by 2 centimeters. Some loose tags of fibrous tissue are attached to the surface. On section the tumor cuts with a fibrous consistence and shows one fairly large cystic area about 1 centimeter in diameter. Scattered over the cut surface are firm, yellow, ground concentric nodules which have the consistence of cartilage. The intervening stroma is tinted in various shades from yellow to brown, the pigmentation being similar to that seen in xanthomatous giant cell tumor.

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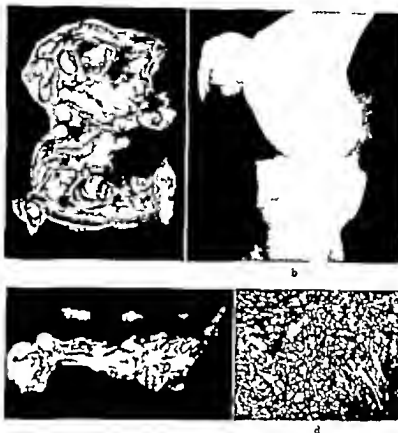


Fig. 4. Case 4. a, Photograph of drawing of bisected specimen, 1/2 actual size. Note the cystic center, the nodular cut surface and the dark pigmentation. b, Roent genogram of original tumor in popliteal space. c, Drawing of specimen, 1/2 actual size, showing recurrent tumor of suprapatellar pouch and articular synovium. d, Photomicrograph, reticulum stain, confirming histiocytic character of tumor. Hematoxylin and eosin sections identical with that in Figure 3c. X75.

The general feature of the disease, the polymorphous aspect of the cells, is typically histiocytic. Because of the second recurrence with extensive invasion of the thigh muscle Berger's Case 5 was treated by disarticulation of the hip.

Case 13 is identical with Case 14. Both of these tumors showed prompt local recurrence; the recurrence in Case 14 being intra-articular and invasive. Neither the recurrence of Cases 13 nor 14 showed xanthoma cells, although they showed classical histiocytic features otherwise similar to xanthomatous giant cell tumor. It is our belief at the present time that these tumors constitute a less malignant variety of synovial sarcoma more likely to prove

locally malignant. On the other hand the tumor showed many features of Case 10 which proved malignant and capable of metastasis. The course of these 2 cases together with Berger's Case 5 will undoubtedly further establish the degree of malignancy of this type.

**CASE 4** Synovium of right popliteal space recurring after 3 months within the knee joint. Treated by local excision, synovectomy and amputation.

C. G., male, aged 46 years, was first seen in the clinic of the Hospital for Ruptured and Crippled on December 6, 1933, complaining of swelling and pain in the right knee beginning 1 month previously without any apparent cause. He had visited physician concerning it, had been given some oral

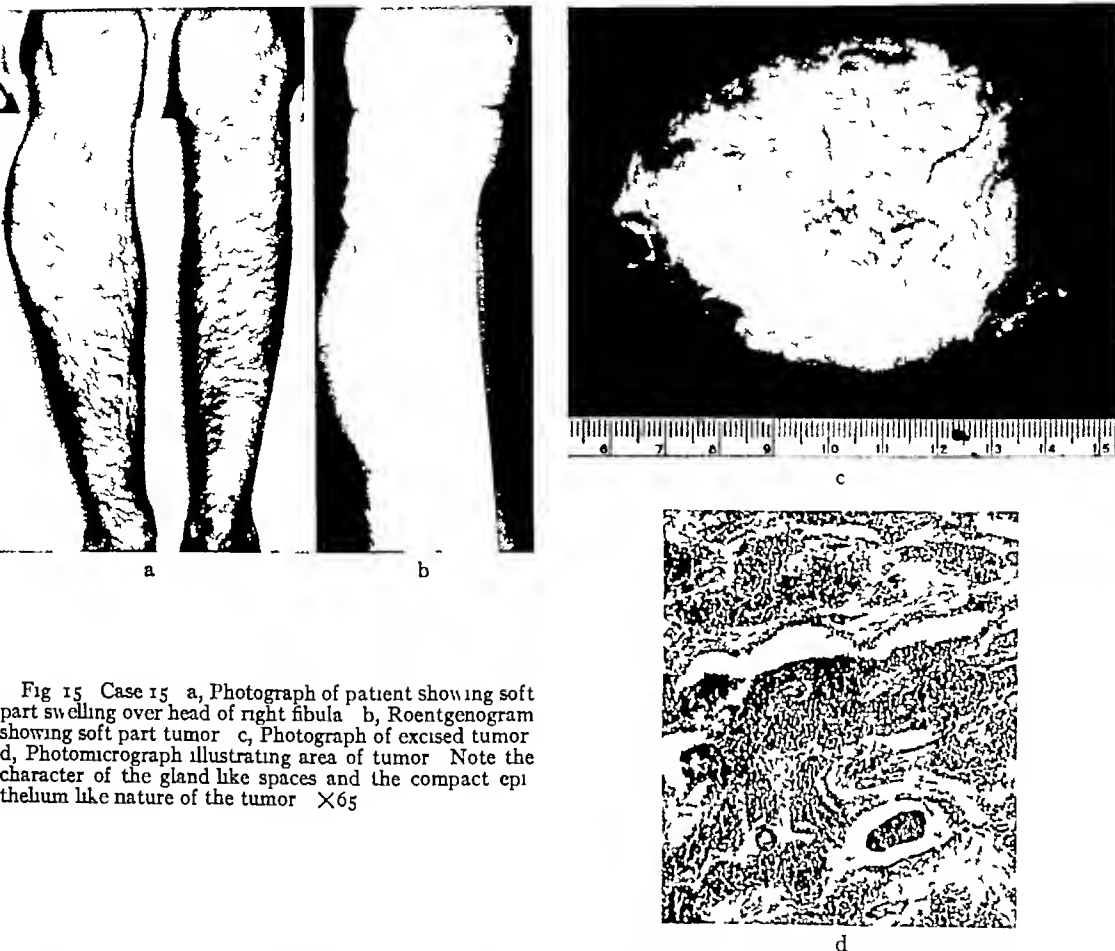


Fig 15 Case 15 a, Photograph of patient showing soft part swelling over head of right fibula b, Roentgenogram showing soft part tumor c, Photograph of excised tumor d, Photomicrograph illustrating area of tumor Note the character of the gland like spaces and the compact epithelium like nature of the tumor  $\times 65$

medication, and swelling subsided after 2 weeks. His past history was negative regarding any important illnesses.

Examination revealed a slight fullness of the entire knee joint, slight ballottement of the patella, and a palpable mass about the size of a walnut in the middle of the popliteal space. This was tense and slightly fluctuant.

Roentgenograms showed fluid within the joint capsule and a well defined density in the popliteal region.

A diagnosis of cyst of popliteal space was made and excision was advised. Patient refused to have this done.

Patient was next seen May 26, 1938, and stated that he had been free from pain until 1 week previous to this visit at which time he had a sudden recurrence of pain and swelling of the right knee. This gradually increased until he was entirely disabled. He had a temperature of 99.2 degrees, diffuse swelling, and generalized tenderness about the knee and some local increase in heat. The previously

noted mass was present in the popliteal space. An aspiration of the knee joint was done and 250 cubic centimeters of a turbid yellowish fluid was obtained. Sedimentation rate was 45 millimeters in 1 hour. The patient was again advised to enter the hospital for excision of the cyst.

On June 1, 1938, the patient consented to operation, and on June 3, 1938, a large firm tumor lying medial to the medial head of the gastrocnemius and originating probably in a semimembranous bursa or tendon was excised.

The specimen was an encapsulated tumor 6 by 4 by 2 centimeters. There was some fat adherent to the capsule. On sagittal section the color was a mottled white and orange and in the center was an area of cystic softening, 1 centimeter in diameter, which contained some jelly like material.

The microscopic features were identical with those in Case 13.

Patient was seen at monthly intervals and occasionally complained of vague aches about the knee. Nine months after operation a mass was noted over



the anterolateral aspect of the right knee in the suprapatella pouch. There was no evidence of recurrence in the popliteal space.

He was readmitted on May 4, 1930.

Examination at this time revealed a healed scar in the popliteal region. Just above and lateral to the patella, there was a mass 4 centimeters in diameter which was firm, freely movable and in the suprapatellar pouch, not tender. There was demonstrable free fluid in the joint.

A diagnosis of recurrent synovoma was made and the patient was operated upon on May 3, 1930, through a large anterior incision. The suprapatellar pouch was found to be filled with a firm pedunculated tumor mass extending back between the condyles of the femur. A total synovectomy was performed and followed by amputation a week later.

The specimen consisted of the resected synovial membrane of the knee joint with some adherent fatty tissue. When laid out, it measured 6 by 10 inches and averaged about  $\frac{3}{4}$  of an inch in thickness. Grossly it contained three chocolate brown firm, nodular pedunculated tags of adherent tumor tissue. These had a firm almost cartilaginous consistency. In addition, there was one large area which was irregular and nodular which was also chocolate brown in color and corresponded to the mass which occupied the suprapatellar pouch. The gross appearance of the specimen was not unlike that of diffuse xanthomatous of the knee joint.

Several microscopic sections of the small fragments were prepared. In general, the recurrence was basically the same as the original tumor.

Patient is alive without evidence of disease May 9, 1930, year after operation.

**CASE 15.** Synovoma probably originating in bursa or tendon sheath of right biceps femoris treated by local excision followed by deep x-ray therapy. Death within 8 months of extensive pulmonary metastases.

E. B., an American male, aged 4 years, was first seen in the New Haven Hospital in April, 1934, when meningioma of the right precentral region was removed. He recovered completely from this operation and in April, 1936 returned to the hospital. Almost since the brain operation a year before the patient had noticed that his right leg was slightly larger than the left. He had noticed in the last 6 weeks that the right leg had definitely increased in size. There was no history of trauma.

On physical examination there was found over the lateral surface of the proximal half of the right lower leg a firm slightly tender nonreddened oval mass, about the size of a orange. The laboratory findings were negative. A diagnosis of sarcoma of the right leg was made the patient was operated upon, and the mass excised. The peroneal nerve was found to course through the mass. The patient made an uneventful recovery, left the hospital approximately 1 month after operation. Following the operation he was given a course of deep x-ray therapy through three ports, medial, lateral, and posterior

through the region of the tumor and also to the right inguinal region. A chest plate at the time of the removal of the tumor failed to reveal any evidence of metastatic tumor. The patient re-entered the hospital in August, 1937, because of complaint of cough and chest pain of about 3 weeks duration. X-ray films revealed the presence of tumor metastases in the mediastinum and accumulation of fluid in both pleural cavities. The pleural fluid contained tumor cells. He expired 11th extensive metastatic tumor on October 4, 1937.

The specimen was an oval mass of three high measures by 7 by 3.5 centimeters. Its external surface was roughened and showed few short tags of muscle and fibrous tissue adherent. The tumor was moderately soft cut readily and revealed pink-gray cut surface the tissue was succulent and friable and in the central portion had a yellow opaque appearance here it had become necrotic. There was a suggestion of thin fibrous tissue capsule about the tumor which appeared to be invaded by tumor in several places.

Microscopic sections from various portions all showed an essentially similar appearance. The tumor was cellular and was composed of cells of fairly uniform size and shape. They were somewhat polyhedral in outline with finely granular pink staining cytoplasm with round or oval basophilic hyperchromatic nuclei. There were one or two mitoses per high power field. In some fields the cells surrounded connective tissue stalks which gave the tumor a papillary architecture. In other places long slit like spaces lined by flattened tumor cells were seen. These were surrounded by masses of the polyhedral cells. A thin fibrous tissue capsule which was invaded by tumor was present. The tumor also invaded the surrounding skeletal muscle and was also present as tumor thrombi in some of the surrounding blood vessels.

The dominant histological feature was the reproduction of neoplastic villi similar to that in areas of Case 1. Other areas suggested reticulum cell sarcoma.

The following case is of interest because it represents one of the few if not the only autopsy record of a synovial sarcoma.

**CASE 16.** Synovoma of right tibial condyle and overlying right lateral epicondyle treated by local excision followed by deep x-ray therapy. Death within 7 months of generalized metastases. Autopsy S. M., an Italian male aged 45 years, was admitted to the New Britain Hospital on May 6, 1938.

On first admission December 6, 1937, he had complained of swelling on the right lateral aspect of the right arm just above the lateral condyle extending medially to the antecubital fossa. He stated that about 3 days previous to this admission he felt a small nodule about the size of the tip of the

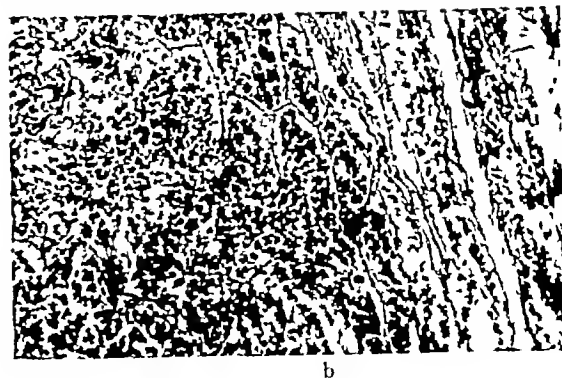


Fig 16 Case 16 a, Nodular pulmonary metastases seen at autopsy b, Photomicrograph of pulmonary metastases,

reticulosarcomatous character  $\times 100$  c, Metastases in right ventricular endocardium, about  $\frac{2}{3}$  actual size

thumb. The nodule grew in size, without associated pain, heat, or redness, and without impairment of motion.

On the right lateral aspect of the right arm about 1 inch above the lateral epicondyle and extending medially toward the antecubital fossa, was a nodular mass about the size of an English walnut. It was not very hard and appeared to be fixed to the deep tissue, but not to the skin.

Biopsy was performed on December 6, 1937. The pathological diagnosis was malignant synovoma, and the patient was discharged on December 10, 1937. Deep x-ray therapy was begun on December 27, 1937.

Examination of microscopic sections revealed a highly cellular tumor composed of a syncytial arrangement of pale endothelium like cells with large oval reniform or rounded nuclei. The arrangement of the tumor was largely perithelial. In areas, however, compact epithelium like cell masses were present.

His second admission was on March 13, 1938, at which time he complained of pain in the back, especially on walking, for the previous 2 or 3 weeks. The

pain was also present posteriorly at both iliac crests. At this time there was some tenderness to pressure over the posterior half of both iliac crests. There was marked point tenderness over the spine at the level of the eleventh and twelfth dorsal vertebrae.

On March 14, x-ray examination of the spine and chest showed two definitely rounded areas in the right lung field, one about the size of a quarter, the other about the size of a silver dollar, both lying in the lower lung field. The left lung showed one soft rounded shadow in the lower portion. There was also destruction of the spinous process of the twelfth thoracic vertebra. Following discharge the patient was admitted to the Memorial Hospital, where further irradiation was given.

His third admission was on May 10, 1938. He complained of excruciating pain in the right lower chest and some pain in the left chest, right sacrum, and lower posterior back. There was also pain in both legs. At this time there was some tenderness of the right upper abdomen and the liver appeared to be enlarged. Palpation of the lower back revealed marked tenderness over the right sacrum and isch-

TABLE I.—ANALYSIS OF 16 CASES OF SYNOVIAL SARCOMA

| Sex | Age at onset | Location  | Pre-operative condition |                |                         | X ray features   | Pre-operative diagnosis | Treatment and course   | Post-operative condition | Microscopic features   |
|-----|--------------|---|-------------------------|----------------|-------------------------|--|-------------------------|--|--------------------------|--|
|     |              |   | Pain                    | Local swelling | Functional interference |  |                         |  |                          |  |
| F   | 17           | Right elbow<br>Para-articular                                   | yes                     | yes            | yes                     | May 1919. Circumscribed tumor showing calcification                            | Sarcoma                 | May 1919. Local excision. Deep incision. Above, with arthrotomy in situ. July 1919 | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases. Primary sarcoma. Primary sarcoma. |
| F   | 17           | Left knee<br>Para-articular                                     | yes                     | yes            | yes                     | Not done   | Tumor                   | August, 1919. Local excision. Above, in situ. July 1920                            | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left elbow<br>Circumscribed tumor                               | yes                     | yes            | yes                     | Not done   | Epithelial sarcoma      | November 1919. Local excision. Above, in situ. May 1920. Second excision           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Right thigh and lower trunk                                     | yes                     | yes            | yes                     | January, 1920. Local excision. Above, in situ. July 1920                       | Epithelial sarcoma      | January, 1920. Local excision. Above, in situ. July 1920                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Articular sarcoma. Para-articular. Popliteal space | yes                     | yes            | yes                     | June, 1920. Increased size. Tumor below patella. M. P. 1920. P. 1920. P. 1920. | Epithelial sarcoma      | June, 1920. Local excision. Above, in situ. July 1920                              | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Para-articular                                     | yes                     | yes            | yes                     | September, 1920. Calcified tumor. Tumor below patella.                         | Tumor                   | September, 1920. Local excision. Above, in situ. July 1920                         | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Right knee<br>Articular and para-articular. Popliteal space     | yes                     | yes            | yes                     | January, 1921. Nodular tumor. Tumor below patella.                             | Tumor                   | January, 1921. Local excision. Above, in situ. July 1921                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | November, 1921. Calcified tumor. Tumor below patella.                          | Tumor                   | November, 1921. Local excision. Above, in situ. July 1921                          | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1922. Local excision. Above, in situ. July 1922                       | Tumor                   | January, 1922. Local excision. Above, in situ. July 1922                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1923. Local excision. Above, in situ. July 1923                       | Tumor                   | January, 1923. Local excision. Above, in situ. July 1923                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1924. Local excision. Above, in situ. July 1924                       | Tumor                   | January, 1924. Local excision. Above, in situ. July 1924                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1925. Local excision. Above, in situ. July 1925                       | Tumor                   | January, 1925. Local excision. Above, in situ. July 1925                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1926. Local excision. Above, in situ. July 1926                       | Tumor                   | January, 1926. Local excision. Above, in situ. July 1926                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1927. Local excision. Above, in situ. July 1927                       | Tumor                   | January, 1927. Local excision. Above, in situ. July 1927                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1928. Local excision. Above, in situ. July 1928                       | Tumor                   | January, 1928. Local excision. Above, in situ. July 1928                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |
| F   | 17           | Left knee<br>Popliteal space                                    | yes                     | yes            | yes                     | January, 1929. Local excision. Above, in situ. July 1929                       | Tumor                   | January, 1929. Local excision. Above, in situ. July 1929                           | 4 mm                     | Epithelial sarcoma. Sarcomatous. Metastases.                                   |

TABLE I.—ANALYSIS OF 16 CASES OF SYNOVIAL SARCOMA—Continued

| Sex   | Age at onset | Location   | Pre-operative symptoms |                |       |          | X ray findings   | Pre-operative diagnosis                                 | Treatment and course   | Post-operative follow-up | Microscopic features   |
|-------|--------------|--|------------------------|----------------|-------|----------|--|---|--|--------------------------|--|
|       |              |  | Pain                   | Fluid swelling | Tumor | Duration |  |   |  |                          |  |
| H N ♂ | 25           | Right knee<br>Articular                                      | 10 yrs                 | 0              | 0     | 10 yrs   | 1924 Articular soft tissue tumor                                       | 1913 to 1924. Synovitis                                 | 1913 to 1924. Conservative treatment February 1924. Resection followed by local recurrence<br>February 1925. Deep x ray. Coley's toxins<br>February 1926. Resection followed by amputation<br>Died 1936 pulmonary metastases | 10 yrs                   | Fibrosarcoma with chondroplasia. Fibroendothelioma.                          |
| R L ♂ | 10           | Left knee<br>Articular and suprapatellar pouch               | 6 yrs                  | †              | 0     | 6 yrs    | April 1915 Suprapatellar tumor unoperated<br>July 1917 Recurrent tumor | April 1915 Synovitis<br>March, 1916 Tumor of quadriceps | March 1916 Local excision<br>October 1917 Excision and deep x ray<br>1890R 3 portals<br>February 1918 With high amputation<br>December, 1918 Died, generalized metastases  | 2 yrs 9 mos              | Fibrosarcoma with chondroplasia and clefts<br>Fibrosarcoma. Reticulosarcoma. |
| F S ♀ | 30           | Right fourth finger<br>Flexor tendoo                         | †                      | 0              | 0     | 6 mos    | Not done   | October 1937 Dupuytren's contracture                    | February 1938 Local excision followed by 24 x ray treatments<br>May 1939 Recurrence midforearm amputation. Alive without evidence of disease<br>December 1939  | 1 yr 10 mos              | First epithelioid giant cell recurrence<br>atypical synovium                 |
| H B ♂ | 48           | Left knee<br>Popliteal space                                 | 0                      | 0              | 1 mo  | 1 mo     | July 1937 Soft part popliteal tumor<br>March 1939 Negative chest plate | 'Tumor'   | July 1937 Local excision<br>November 1937 Recurrence and second excision. Alive without evidence of disease<br>July 1940   | 3 yrs                    | Chondromatous giant cell tumor<br>features Reticulosarcoma synovial spaces   |
| C G ♂ | 46           | Right knee<br>Articular and semimembranosus bursa and tendon | 2 yrs                  | 2 yrs          | 0     | 2 yrs    | December 1937 Fluid swelling in knee joint                             | 'Popliteal cyst'  | May 1936 Aspiration of joint<br>June 1938 Excision<br>March 1939 Synovectomy for intra-articular recurrence followed by amputation<br>Alive without evidence of disease<br>December 1940                                     | 3 yr 6 mos               | Chondromatous giant cell tumor<br>features Synovial spaces                   |
| E B ♂ | 40           | Right knee<br>Bursa of biceps femoris                        | 0                      | 0              | 2 yrs | 0        | April 1936 Soft part tumor<br>October 1937 Pulmonary metastases        | Fibrosarcoma  | April 1936 Excision and deep x ray to right groin<br>October 1937 Pulmonary metastases and death   | 18 mos.                  | Popliteal neoplastic synovial Reticulosarcoma.                               |
| S M ♂ | 45           | Right elbow<br>Para articular                                | 0                      | 0              | 1 mo  | 0        | March 1938 Pulmonary and spinous metastases                            | 'Tumor'   | December, 1937 Local excision and deep x ray<br>March 1938 Deep x ray to skull and spine for pulmonary, cranial and vertebral metastases<br>Died May 1938  | 5 mos                    | Reticulosarcoma.   |

tum. There was an area of tanning of the lower back where the patient had received x-ray therapy. His temperature fluctuated between 90 and 100 degrees. During the last week, it was constantly elevated and ranged between 100 and 103 degrees. On this admission there was a bald area on the right side of the scalp where there had previously been a tumor. There was also a tender mass about the size of a large walnut over the left parietal region. Deep x-ray therapy was continued but the patient's condition became worse. On May 23d, while going to the bathroom he placed his arm on the door and sustained a pathological fracture.

He continued to complain bitterly of pain in the right sacrum and right leg. Antispasmodic treatment was administered in three doses with marked relief of the pain. He continued to fall however and on June 3 became comatose. He expired on June 14, 1938.

Clinical diagnosis: Malignant synoviomatosis of the right elbow with multiple metastases to lung and bones.

Autopsy examination was permitted. Subject was an emaciated, dolt, white male, weighing 100 pounds, body length, 164 centimeters.

Two soft rounded fluctuant tumor nodules were located in the right and left parietal regions. In the right upper extremity about 3 centimeters above the lateral condyle there was a firm, rounded mass not attached to the skin. Medially and anteriorly above the antecubital space was a smaller, similar nodule about 1 centimeter in diameter. The large nodule was located near the upper end of the humerus near which represented the site of the previous operative incision. There was a fracture of the upper third of the left humerus.

When the abdominal cavity was opened, a small, firm hemorrhagic red nodule 1/4 centimeters in diameter was found in the greater omentum, and several similar but smaller nodules were found on the lesser omentum near the attachment to the stomach.

One nodule was found in the right ventricle and one in the left ventricle of the heart.

Both lungs were large, heavy and studded with innumerable nodular metastases.

The pancreas showed an area of tumor tissue invading the tail of the organ.

There were no metastases to the liver, adrenals, spleen, kidneys, or gastro-intestinal tract.

Nodular metastases occupied the fifth, sixth, seventh, and twelfth ribs.

Summary of the findings, therefore, indicates local recurrence of the tumor with widespread metastases to the lungs, heart, pancreas, ribs, dorsal vertebra, omentum, scalp, and left humerus.

In the metastases of the tumor as seen in the lung, the tumor was composed of small, rounded nuclear elements about the size of lymphocyte supported by a fine delicate reticulum. Here the aspect was typical of certain forms of reticulosarcoma.

## SUMMARY

A study of the 16 personally observed cases of synovial sarcoma comprises the largest single series to be reported in the literature and enables one to draw certain conclusions of the clinical course and histological behavior of this condition.

Histologically all the varieties of synovial sarcoma, however extreme and variable they may appear to be, exhibit specific characteristics which permit of their identification. Nor is the time far distant when the malignancy and radiosensitivity of this tumor will be graded as accurately as is now possible for other malignant tumors.

The evolution of all synovial sarcomas may be correlated with various functional and histological characteristics of normal synovial tissue. The characteristics previously mentioned are here reiterated.

1. An endothelial structure and function. The lining synovial cell represents a differentiated form of synovial histiocyte destined to play a border or endothelial function. In the synovial sarcoma, the endothelial function is frequently exhibited as glandlike spaces resembling adenomasarcoma, as sheets or nests of epithelium-like cells, as neoplastic villi or as well differentiated synovial borders. In order of malignancy these tumors appear to lie midway between the classical histiocytic tumors and the reticulosarcomas (Grades 2-3).

2. A histiocytic structure and function. Normal synovial tissue develops as a histiocytic tissue in the embryo where numerous argyrophilic threads are present. In adult life this histiocytic property persists, and is exemplified by lipophagic, siderophagic, and anthrophagic potentialities. The histiocyte is a relatively totipotent mesenchymal element and is capable of wide ranges of differentiation and dedifferentiation. Microscopically the histiocytic tumors exhibit themselves in several forms. A classical polymorphous histiocytic aspect with giant cells, intracellular inclusions of blood pigment as tumors with classical giant cell features, not greatly different from xanthomatous giant cell tumor. Islands of xanthoma cells may be occasionally present. The behavior of this variety of syn

ovial sarcoma suggests malignancy of a low order (Grades 1-2)

3 Synovial sarcoma may appear as a de-differentiated fibroblastic tumor generally indistinguishable from fibrosarcoma or spindle cell sarcoma unless synovial clefts or small areas of reticulo-endothelial evolution are located. Identification requires multiple sections and careful differential staining. The malignancy of this type would appear to follow closely that of fibrosarcoma and spindle cell sarcoma. In general, slow growth and late metastases is the rule. Moreover, calcification, chondrification, and ossification probably succeed a type of albuminoid impregnation of the tumor and when present in a tumor whose location suggests a synovial origin, should lead to further attempts to establish the specificity of the tumor.

4 Mucin formation is not infrequently exhibited in synovial sarcomas and appears to be confined to the endothelial cell components.

5 Clinically, synovial sarcomas in knee joints extend over a long insidious pre-operative course covering an average period of 5-6 years. The surgeon therefore has a reasonably long period in which to institute radical therapeutic procedures and must be ever on the alert for atypical forms of so called synovitis.

6 Synovial sarcomas in other para-articular regions manifest themselves more readily as soft part tumors usually after an average period of a few to several months. The poor end-results are undoubtedly caused in part by the procrastination of the patient and of the surgeon.

7 Amputation is the treatment of choice for all synovial sarcomas. It may be justifiable in instances when the tumor is small and encapsulated, to perform wide local excision and defer amputation until pathological examination has permitted time for histological study. Amputation should never be deferred beyond the time of the first recurrence.

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#### BIBLIOGRAPHY

1. BERGER, LOUIS. Synovial sarcoma in serous bursal and tendon sheaths. *Am J Cancer*, 1938, 34: 501.
2. BLACK, W. C. Synovioma of the hand. *Am J Cancer*, 1936, 28: 481.
3. BRODERS, A. C., HARGRAVE, R., and MEYERDING, H. W. Pathological features of soft tissue fibrosarcoma. *Surg, Gynec & Obst*, 1939, 69: 267.
4. COLEY, BRADLEY L. Personal communication.
5. COLEY, BRADLEY L., and PIERSON, JOHN C. Synovioma. *Surgery*, 1937, 1: 113.
6. DE SANTO, D. A., and WILSON, P. D. Xanthomatous tumors of joints. *J Bone & Joint Surg*, 1939, 21: 531.
7. EWING, JAMES. Personal communication before Third International Cancer Congress.
8. FRANCESCHINI, P. Ricerche istologiche sulle articolazioni. *Arch ital di anat & di embriol*, 1929, 27: 76.
9. GESCHICHTER, C. L., and COPELAND, M. M. Tumors of Bone. 2d ed. *Am J Cancer*—1936.
10. HODGSON, F. G., and BISHOP, E. L. Malignant synovioma of the knee joint. *J Bone & Joint Surg*, 1935, 17: 184.
11. KEY, J. A. In Cowdry's Special Cytology. Vol. 2. New York: Paul B. Hoeber, Inc., 1932.
12. KNOX, L. C. Synovial sarcoma. *Am J Cancer*, 1936, 28: 461.
13. LEJARS and RUBENS DUVAL. Les sarcomes primitifs des synoviales articulaires. *Rev de chir*, 1910, 41: 751.
14. LEWIS, RAYMOND W. Roentgen recognition of synovioma. *Am J Roentgenol*, 1940, 44: 170.
15. SABRAZES, J., and DE GRAILLY, R. *Gaz hebdomadaire de médecine et de chirurgie*, 1932, 53: 449.
16. SABRAZES, J., LOUBAT, E., and DE GRAILLY, R., and MAGENDIO, J. *Gaz hebdomadaire de médecine et de chirurgie*, 1932, 53: 481, 513, 1934, 55: 754.
17. SABRAZES, J., MONTPELIER, J., and DUBOECHE, R., and DE GRAILLY, R. *Gaz hebdomadaire de médecine et de chirurgie*, 1932, 53: 769.
18. SENEAR, F. E., and CARO, M. R. Histiocytoma cutis. *Arch Dermat & Syph*, 1936, 33: 209.
19. SMITH, A. D. F. Personal communication.
20. SMITH, L. W. Synoviomata. *Am J Path*, 1927, 3: 355.
21. STUER. Cited by Berger and Sabrazes.
22. SIMMONS, CHANNING C. Bone sarcoma. *Surg, Gynec & Obst*, 1939, 68: 67.
23. VAUBEL, E. Form and function of synovial cells in tissue cultures. *J Exper Med*, 1933, 58: 63-85.
24. WAGNER, L. C. Intra articular endothelial tumors arising from synovial membrane. *Ann Surg*, 1930, 91: 421.
25. WARREN, SHIELDS, and SOMMER, G. N. F. JR. Fibrosarcoma of soft parts. *Arch Surg*, 1936, 33: 425.

# BACTERIAL FLORA OF ACUTE TRAUMATIC WOUNDS

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**T**RAUMATIC wounds present conditions in regard to the possibility of infection which are quite different from those ordinarily encountered in aseptic surgery. Bacteria, both aerobic and anaerobic, are carried into the tissues from the surrounding skin as well as on clothing and other foreign bodies introduced by the agents producing the trauma. Tissues are destroyed to a variable degree and such devitalized tissues furnish an excellent medium for bacterial growth. Certain of the contaminating bacteria may produce a violent spreading infection including the dreaded gas gangrene. Bacterial cultures, therefore, become a necessary basis for the intelligent treatment of accidental wounds. This study concerns itself with the analysis of the bacterial flora cultivated from 200 acute traumatic previously untreated wounds.

The older studies on the bacteriology of accidental wounds were in many instances inadequate because of lack of satisfactory anaerobic and aerobic methods of cultivation. The means of obtaining the cultures were not always such as to bring to light every type of organism present. Often cultures were secured from only one part of the wound and without the benefit of anaerobic bacteriological studies.

Riggenbach (1898) was probably the first to suggest the importance of anaerobes as well as aerobes in accidental wounds. His method was to swab the surface of the wound with cotton which was inoculated into broth, one-half being incubated aerobically and one-half anaerobically. From 24 cases he isolated *Staphylococcus albus*, 14 times; *Staphylococcus aureus*, 4 times; streptococci (kind not mentioned) 6 times; *Micrococcus tetragenus*, 5 times; pneumococci, twice; *Friedländer's bacillus* and *Bacillus coli* once each. *Clostrid-*

*ium tetani* was seen twice. No mention is made of other anaerobes. He found that all the wounds showed a mixed flora, either with saprophytes which were easily identified or sometimes, with unknown rods and cocci. He concluded that wounds may contain pathogenic bacteria without clinical evidence of infection, these disappearing as healing progresses.

There is an enormous literature on the bacterial flora of war wounds of the First World War (3). These studies are important in that they directed attention to the frequency with which gas gangrene producing anaerobes could be cultivated from wounds, especially the deep puncture wounds and muscle traumatism in which soil, clothing shrapnel, etc. were implanted in the depths of the wound. The bacterial flora present varied according to the type of injury, the technique for cultivating the organisms, the manner in which the cultural material was obtained, the time interval from injury to the making of the culture, et cetera. Another important contribution from these studies was the observation that a combination of gas gangrene organisms with hemolytic streptococci produced a more virulent gangrenous infection than the anaerobes alone. Zetser (1928) reported 21 cases of traumatic injuries in which anaerobes were isolated in each case. In 3 anaerobes were present without clinical evidence of anaerobic infection. In 8 cases there were anaerobes found with clinical evidence of infection and recovery. In the 10 remaining cases the anaerobic infections were fatal. Anaerobes alone were isolated from 13 of the wounds. Aerobes and anaerobes were combined in the 8 others. The anaerobes grown were *Clostridium welchii*, 21 cases; *Clostridium oedematiens*, 7 cases; *Vibrio septique*, 1 case; *Clostridium histolyticum*, 1 case; *Clostridium tetani*, 3 cases. Of the nonpathogens there were *Clostridium tertium*, 4 cases; *Clostridium sporogenes*, 5

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cases, and *Clostridium bifermentans*, 1 case

Sas (1930) studied 55 accidental wounds, a few minutes to 20 hours after injury—in most cases one-half hour's duration—by introducing two sterile silk knots into the wound "until they were saturated with the wound secretions," then culturing the knots aerobically and anaerobically. The pyrogallic acid-alkali method for culturing anaerobes was used. He isolated *Staphylococcus albus*, 23 times, 41.8 per cent, streptococci (kind not mentioned), 19 times, 34.5 per cent, *Staphylococcus aureus*, 11 times, 20 per cent, *Bacillus coli* group, 5 times, 9 per cent, *Staphylococcus citreus*, twice, 3.6 per cent, pneumococci, twice, 3.6 per cent, gas producing anaerobes, 11 times, 20 per cent. Eight of the anaerobes were identified as *Clostridium welchii*. Not all of the bacteria could be identified. Among the saprophytes were found 16 bacilli, 23 cocci, 7 sarcinae, 1 streptothrix. He concluded that accidental wounds are always contaminated and are more serious than clean operative wounds, especially because gas gangrene producing bacilli may be present without any manifest infection.

Veraart and Dreuth (1930) cultured swabs from secretions of 215 fresh, previously untreated wounds with the following results: 41 per cent of the cases were sterile, 15.5 per cent yielded 100 or more colonies of bacteria. After intensive cleaning with hydrogen peroxide, dilute spirits and ether, then 5 per cent tincture of iodine, 86.5 per cent were sterile and in the remainder there were no wounds which showed more than 100 colonies.

Dimitza and Gutscher (1933) studied 424 wounds by culturing all the excised tissue débrided. Ninety-two cases were found bacteria-free. The 332 others showed staphylococci alone in 108 cases, and mixed with streptococci and colon bacilli in 59 cases, streptococci alone in 31 cases, and mixed with staphylococci and colon bacilli in 62, colon bacilli alone in 10 cases, and mixed with staphylococci and streptococci in 21, *Clostridium welchii* in 57 cases. They believe that the high incidence of *Clostridium welchii*, 20 per cent, indicates that gas gangrene must always be reckoned with, especially in railroad and street accidents, all cases of which showed contamination with

these organisms. However, gas gangrene did not develop in all these cases, clinical symptoms having occurred in only 8. The *Clostridium tetani* was isolated twice, both times from street accident cases, but tetanus did not develop in either.

Sviridov (1936) studied both bacteriologically and clinically 120 acute traumatic wounds before and after épluchage and débridement, by direct smear of the wound surface at the level of the skin, the muscle and bone, and by cultures from the same levels. Anaerobic cultures were not made because of lack of equipment. There were 45 skin wounds, 38 skin and muscle, and 37 skin, muscle, and bone injuries. One hundred cases were treated by épluchage and 20 by débridement. In 100 cases before épluchage he found streptococci (kind not noted) in 13 cases, staphylococci in 25 cases, diplococci in 5 cases, staphylococci with streptococci in 8 cases, streptococci with diplococci in 6 cases, streptococci, diplococci, and staphylococci in 1 case, *Bacillus coli* in 7 cases, *Bacillus subtilis* in 14 cases, other cocci in 21 cases, yeast cells in 2 cases, other saprophytes in 71 cases. After épluchage 27 cases showed pathogenic flora, 28 saprophytes only, and in 45 cases no growth was obtained. Eighty-three of the cases healed by primary intention and 17 suppurred. In the latter staphylococci were grown 5 times, streptococci, 3 times, streptococci with staphylococci, 2 times, and *Bacillus coli* in 1 case. After épluchage 15 per cent of the cases which healed by primary intention gave growth on culture, yet infection did not take place. All these were face and skull wounds. Wounds in this area possess greater resistance to infection and heal by primary intention in 86 per cent of the cases. Wounds of the thigh, shoulder, and pelvis with muscle and bony involvement give the most unsatisfactory results, due to the frequent inability to remove completely all the contaminated tissue. In 20 débrided wounds 1 case of gas gangrene and 1 case of osteomyelitis developed. Both recovered.

Levaditi (1939), during the present World War, cultured wound secretions on cotton swabs from 68 wounds, including 35 flesh wounds, 22 compound fractures, 7 accidental wounds, and 4 amputations, 75 per cent of



TABLE L—BACTERIAL FLORA OF 102 "CLEAN" AND 96 "DIRTY" WOUNDS ACCORDING TO DURATION OF INJURY

| Time from injury to culture                     | 1' |    | 2' |    | 3' |    | 30' |    | 1 hr |    | 2 hr |    | 4 hr plus |    | C.        |           |
|---|----|----|----|----|----|----|-----|----|------|----|------|----|-----------|----|-----------|-----------|
|   | C  | D  | C  | D  | C  | D  | C   | D  | C    | D  | C    | D  | C         | D  | Total     | Total     |
| No. of cases                                    |    |    |    |    |    |    |     |    |      |    |      |    |           |    | %         | %         |
| <i>Staphylococcus albus</i>                     | 24 | 1  | 2  | 18 | 6  | 1  | 10  | 1  | 26   | 20 | 1    | 1  | 1         | 1  | 77 (51.4) | 6 (26.1)  |
| <i>Staphylococcus aureus</i>                    | 24 | 24 | 20 | 12 | 20 | 12 | 17  | 20 | 20   | 12 | 20   | 20 | 20        | 20 | 35 (24.9) | 4 (5.0)   |
| <i>Streptococcus hemolyticus, aerob.</i>        | 17 | 12 |    | 10 |    | 8  |     |    |      |    |      |    |           |    | 46 (31)   | 14 (14.1) |
| <i>Streptococcus hemolyticus, anaerobic</i>     | —  | —  | 6  | 5  | —  | 8  | —   | —  | —    | —  | —    | —  | —         | —  | ( 9 )     | ( 1 )     |
| <i>Streptococcus, non-hemolyticus, aerob.</i>   | 12 |    | 21 | 9  | 5  | 12 | 21  | 1  | 20   | —  | 20   | —  | 20        | —  | 10 (6.4)  | 11 (11.5) |
| <i>Streptococcus, non-hemolyticus, anaerob.</i> |    |    |    | 2  | 7  | —  | —   | 5  | —    | 20 | —    | —  | —         | 12 | 4 (5.8)   | ( 1 )     |
| <i>Streptococcus viridans</i>                   |    |    | 20 | —  | —  | 8  | —   | 6  | 7    | 1  | —    | —  | —         | 20 | 21 (12)   | 12 (12)   |
| <i>Clostridia</i>                               |    |    |    |    | 17 | 6  | 25  | 12 | 20   | 22 | —    | 20 | 20        | —  | 71 (41)   | 12 (12.4) |
| <i>Enterobacteria</i>                           | 17 |    |    | 12 | 20 | 4  | 25  | 2  | 25   | 20 | 20   | 20 | 20        | —  | 22 (12)   | 10 (10.4) |
| <i>Aerobae gram-negative bacilli</i>            | —  | —  | 6  | —  | —  | 12 | —   | —  | —    | —  | —    | —  | —         | —  | ( 9 )     | ( 1 )     |
| <i>Gram-positive aerobic non-hemolytic</i>      | 27 | 1  | 15 |    | 17 | 23 | 26  | 23 |      | 20 | 20   | 20 | 20        | —  | 22 (12.2) | 21 (21.4) |
| <i>Mycetozoa</i>                                | 8  |    | 26 | 8  | 4  | 8  | 26  |    | 5    | 20 | 20   | 20 | 20        | 26 | 20 (19.2) | 10 (10.4) |
| <i>Diphtheroids</i>                             | —  | —  | 6  |    | 6  | 12 | —   | —  | —    | —  | —    | —  | —         | —  | 12        | ( 12 )    |
| <i>Gram-negative cocci</i>                      | —  | —  | 1  | —  | —  | —  | —   | —  | —    | —  | —    | 20 | 20        | —  | ( 2 )     | ( 2 )     |

the cases contained 3 bacterial species or less 1 case was sterile, and the others contained 4, 5 or 6 species. The types of organisms isolated were staphylococci 85 per cent, streptococci (kind not stated) 58 per cent, *Escherichia coli*, 41 per cent, enterococci 28 per cent, *Clostridium welchii*, 17 per cent, *Bacillus pyocyaneus*, 7 per cent. Other types commonly isolated were *Sarcinae*, *Bacillus subtilis* and *Bacillus proteus*.

Rathcke (1940) studied excised tissue fragments from 140 wounds. (*Clostridium tetani*) pathogenic for mice, were isolated from 6 wounds—1 street accident, 2 agricultural 1 sport 1 railroad and 1 glass injury. Other organisms found were various clostridia (kind not mentioned) 22 times staphylococci, 109 times streptococci (kind not mentioned) 28 times *Bacillus coli*, 7 times aerobic spore bearing rods, 29 times gram positive non spore bearing rods 16 times diphtheroids, 16 times enterococci, 8 times actinomycetes, once other bacteria, 5 times. Two wounds yielded

no growth. He recommends prophylactic anti tetanus serum for all accidental injuries.

The results obtained by the different authors presented are difficult to compare because of the lack of uniformity of method of selecting material for examination. The studies of Veraart and Dreuth, and Dimira and Gutacher are surprising as regards the large number of cases from which sterile cultures were obtained. It might have enhanced the value of these investigations had the distinction been made between clinically clean and dirty wounds likewise any relationship between the types of contaminating organisms and the age of the wound. In this study we have attempted to evaluate some of these factors.

#### MATERIAL AND TECHNIQUE

Fresh, accidental wounds, both in ambulatory and hospitalized cases, were studied. Cases of patients who had any form of treatment prior to arrival in the hospital were not included. The material for study was collected

TABLE II—BACTERIAL FLORA OF 200 ACUTE TRAUMATIC WOUNDS

| Time from injury to culture                   | 5    | 10   | 15   | 20   | 30   | 45  | 60   | 60 plus | Total | %    |
|---|------|------|------|------|------|-----|------|---------|-------|------|
| No. of cases                                  | 36   | 49   | 38   | 15   | 33   | 10  | 7    | 12      | 205   |      |
| <i>Staphylococcus albus</i>                   | 60.4 | 81.6 | 80.4 | 80   | 78.7 | 100 | 100  | 81.3    | 162   | 81   |
| <i>Staphylococcus aureus</i>                  | 5.8  | 51   | 42.1 | 53.3 | 54.6 | 60  | 57.1 | 83.3    | 104   | 52   |
| <i>Streptococcus hemolyticus aerobic</i>      | 25   | 12.2 | 2.6  | 6.7  | 6.1  | —   | 42.8 | 25      | 25    | 12.5 |
| <i>Streptococcus hemolyticus microaerobic</i> | —    | 6.1  | 2.6  | 13.3 | 6.1  | 10  | —    | —       | 9     | 4.5  |
| <i>Streptococcus nonhemolytic, aerobic</i>    | 30.5 | 16.3 | 23.7 | 20   | 15.1 | 20  | 14.2 | 16.7    | 40    | 20   |
| <i>Streptococcus nonhemolytic, anaerobic</i>  | 2.8  | 8.1  | 5.2  | —    | 9.1  | 20  | —    | 8.3     | 13    | 6.5  |
| <i>Streptococcus viridans</i>                 | 11.1 | 6.1  | 13.1 | 6.7  | 9.1  | —   | —    | 16.7    | 18    | 9    |
| <i>Clostridia</i>                             | 11.1 | 8.1  | 23.7 | 20   | 33.3 | 30  | 85.7 | 41.6    | 46    | 23   |
| <i>Enterobacteria</i>                         | 16.7 | 20.4 | 34.2 | 26.6 | 12.1 | 40  | 28.5 | 25      | 46    | 23   |
| Anaerobic gram negative bacilli               | —    | 4    | —    | 6.7  | —    | —   | —    | —       | 3     | 1.5  |
| Gram positive aerobic spore bearing bacilli   | 44.4 | 36.8 | 44.7 | 26.6 | 36.3 | 30  | 42.8 | 50      | 80    | 40   |
| Micrococci                                    | 11.1 | 26.5 | 21   | 20   | 18.1 | 40  | 57.1 | 33.3    | 49    | 24.5 |
| Diphtheroids                                  | 2.8  | 2    | 6.3  | 6.7  | 3    | —   | —    | —       | 7     | 3.5  |
| Gram negative cocci                           | —    | 2    | —    | —    | —    | —   | 28.5 | —       | 4     | 2    |

in the Accident Room and Surgery of the Frankford Hospital, Philadelphia, Pennsylvania, and the Emergency Ward of the Presbyterian Hospital, New York. The types of wounds included deep and trivial lacerated wounds, bullet, dog and human bite and other puncture wounds, machine and automobile accidents, traumatic amputations, and compound fractures. Most of the cases were lacerated wounds. Many were street accidents. The time period from injury to culture varied from a few minutes to 24 hours. The majority of cases comprised patients seen within one-half hour of the time of injury. It was difficult to obtain study material on cases longer than 1 hour's duration. Most of such patients had some form of antiseptic treatment applied en route to the hospital.

In collecting material we wished to cultivate not only the contaminating organisms deposited on the surface of the wound but also those lodged in the crevices and interstices. It was decided therefore to excise the traumatized tissue to the extent that it was representative of the wound as a whole, and to culture the excised tissue *in toto*. All our cultures, therefore, represent the bacterial flora present in tissue fragments débrided under general or local anesthesia, and prior to the institution of any treatment. As soon as the tissue was débrided it was introduced into tubes or flasks of liquid

culture media. Rosenau's brain dextrose medium was first used. Later thioglycollate (1) media was substituted, its use obviating the necessity of preheating the media to drive off the contained air. We found the thioglycollate medium satisfactory for our purposes. The inoculated media was then taken to the laboratory accompanied by a slip stating the site, extent, and duration of the injury, with notation as to whether the wound appeared clean or dirty. We consider swab cultures inadequate.

The cultures were incubated overnight. If any failed to show turbidity, further incubation was done. The contents were mixed by means of a Pasteur pipette and a portion of the culture was removed and streaked on a pair of 5 per cent sheep's blood agar Petri plates. Another drop was placed on a glass slide for Gram stain. One plate was incubated aerobically and the other anaerobically in a McIntosh-Fildes type jar, evacuated to 350 millimeters mercury by means of a water pump, then slowly filled with hydrogen streaming over heat-activated palladiumized asbestos until a positive pressure was obtained. The aerobic plates were examined the next day, the anaerobic plates usually after 48 hours' duration. If there was no growth, the incubation of negative cultures was continued for 48 hours. When growth appeared on the plates, all the various colony types were fished and identi-

fied in the usual way by morphological and cultural studies. Most cultures were replated before discarding for check on the original findings. Virulence tests on pathogens groupings of the hemolytic streptococci, and coagulase tests on the staphylococci were not made. Molds and fungi were not identified.

### RESULTS

Two hundred cases were studied, comprising 102 clinically clean cases, and 98 "dirty" or foreign body contaminated cases. The findings in the number of cases procured in each time period are presented in Tables I and II. The distribution of cases according to aerobic and anaerobic organisms cultivated is presented in Table III.

TABLE III.—AEROBIC AND ANAEROBIC ORGANISMS ISOLATED

|                        | Clean |          | Dirty |          | Total |          |
|------------------------|-------|----------|-------|----------|-------|----------|
|                        | Cases | Per cent | Cases | Per cent | Cases | Per cent |
| Aerobes alone          | 66    | 76       | 52    | 54       | 118   | 66.5     |
| Anaerobes alone        |       |          |       |          |       | 6        |
| Aerobes plus anaerobes |       | 6        | 42    | 41.8     | 42    | 33       |
|                        | 102   |          | 98    |          | 200   |          |

The clinically "clean" cases predominate in the 5 and 10 minute groups, while in the older wounds there were more of the "dirty" cases. Six hundred and six different bacterial species were cultivated, making an average of 3 per wound. Aerobes alone were present in 133 cases or 66.5 per cent of the total. Anaerobes alone were cultivated from only 3 cases, 1.5 per cent dirty wounds. Aerobes plus anaerobes were grown from 64 wound débridements, 32 per cent of total. All of the wounds studied yielded positive cultures. This is in contrast to the reports of Dumke and Gutacher who found 92 wounds sterile 21.7 per cent, in a total of 424; the technique for study being similar to this one and to those of Veerhaart and Dreuth who reported 41 per cent of the cultures of 215 cases, sterile by the cotton swab method.

Anaerobes were present in 22 of the "clean" cases, 21.6 per cent of total, as against 42 of the dirty cases, 43.5 per cent of total. The

presence of foreign bodies in dirty wounds, especially street dirt undoubtedly contributes to the preponderance of anaerobes.

The percentage of anaerobes increased with the older wounds. Mason believes that organisms from human sources contaminating wounds usually gain entrance after rather than at the time of injury and that they may be introduced by the application of a soiled dressing or by handling the wound without proper aseptic precautions. It may be conjectured that these factors explain the increase in anaerobes noted in the older wounds.

**Staphylococci** From the foregoing tables it is evident that these organisms can be isolated from nearly every wound. As is well known, however staphylococci can be cultivated at will from the unbroken skin. The *Staphylococcus albus* was isolated 162 times, 81 per cent of cases, and the *Staphylococcus aureus* from 104 wounds, 52 per cent of cases. The distribution of both *Staphylococcus aureus* and *Staphylococcus albus* was about equal between the clean and dirty cases. Pigmentation is by itself of limited value in the differentiation of staphylococci. Division on the basis of hemolysis and production of human plasma coagulase has recently been shown to be advantageous, and in future studies this classification will be adopted. Staphylococci were found alone in only 7 instances. Associated with *Staphylococcus aureus* in 99 cases were *Staphylococcus albus*, 78 times streptococci, 55 times (hemolytic, 17 green, 11 nonhemolytic, 27) gram positive aerobic spore bearing bacilli 33 times clostridia, 23 times enterobacteria, 11 times micrococci and sarcinae 29 times. Anaerobic organisms were isolated in conjunction with *Staphylococcus aureus* 33 times.

**Streptococci** Next in frequency to the staphylococci, streptococci were recovered from 101 wounds, 50 per cent, 105 isolations were made. The nonhemolytic variety accounted for 53 of this number 40 being aerobic and 13 anaerobic. The hemolytic streptococcus was grown from 34 cases—aerobic, 25 microaerophilic, 9. Green streptococci were cultivated 18 times. The distribution is of interest. The clinically clean wounds showed the nonhemolytic streptococcus in 35 cases, 33.3 per cent (aerobic, 29 anaerobic, 6) and

the hemolytic species in 9 cases, 9 per cent. However, in the dirty cases, the hemolytic streptococcus was isolated 25 times—aerobic, 18, microaerophilic, 7, 25 4 per cent—while the nonhemolytic variety was found 18 times, 18 2 per cent. The green streptococci were found in the same proportion in clean and dirty cases. Pure cultures were rarely found. The organisms commonly isolated with the streptococcus are given in Table IV. It would have been of considerable interest to have grouped the hemolytic streptococci according to Lancefield's classification.

TABLE IV — ORGANISMS COMMONLY ISOLATED WITH THE STREPTOCOCCUS

|                              | Staphylococcus albus | Staphylococcus aureus | Hemolytic streptococcus R | Hemolytic streptococcus N | Nonhemolytic streptococcus R | Nonhemolytic streptococcus N | Green streptococcus | Clostridia | Enterobacteria | Bacillus subtilis group | Total cases |
|------------------------------|----------------------|-----------------------|---------------------------|---------------------------|------------------------------|------------------------------|---------------------|------------|----------------|-------------------------|-------------|
| Nonhemolytic streptococcus R | 32                   | 20                    | 1                         | 0                         | —                            | 0                            | 1                   | 7          | 7              | 8                       | 40          |
| Nonhemolytic streptococcus N | 12                   | 5                     | 1                         | 0                         | 0                            | —                            | 1                   | 2          | 2              | 5                       | 13          |
| Hemolytic streptococcus R    | 19                   | 14                    | —                         | 0                         | 1                            | 1                            | 1                   | 12         | 2              | 13                      | 25          |
| Hemolytic streptococcus N    | 8                    | 4                     | 0                         | —                         | 0                            | 0                            | 0                   | 1          | 2              | 3                       | 9           |
| Green streptococcus          | 11                   | 12                    | 1                         | 0                         | 1                            | 1                            | —                   | 2          | 2              | 6                       | 18          |

R—aerobic  
N—anaerobic

*Clostridia*. This important group of organisms was isolated from 46 cases, 23 per cent of total. They contaminated the dirty wounds 3 times as frequently as the "clean" ones—34 6 per cent as against 11 1 per cent. Interestingly, the older the wound the more frequently were clostridia isolated from it. The same held true for the "clean" as well as the dirty wounds. The varieties isolated included *Clostridium welchii*, 24 times, *oedematiens* (novyi), twice, *bifermentans*, once, *multifermentans*, 3 times, *histolyticum*, twice, *aerofetidum*, once, *tetani*, 3 times, *tertium*, 3 times, *sporogenes*, twice, *botulinum*, once, *chauvei*, once, not identified, 3. The organisms isolated with the clostridia were *Staphy-*

*lococcus albus*, 39 times, *Staphylococcus aureus*, 22 times, streptococci, 24 times, gram positive aerobic spore-bearing bacilli, 17 times, enterobacteria, 8 times. No cases of gas gangrene and no cases of tetanus infection developed in the wounds from which these organisms were grown, treatment being instituted to prevent their activity. While the presence of these organisms in a wound does not guarantee infection, their high incidence is a forceful argument for keeping this possibility constantly in mind and for taking any possible steps to avoid it.

*Enterobacilli*. Forty-nine, or 24 5 per cent, of the wounds studied showed gram negative bacilli on cultivation, their presence being about equal in both the clean-looking and the dirty wounds. They were cultivated most commonly from hand and leg wounds, and least frequently from scalp wounds. The varieties isolated included *Escherichia*, 13, *Proteus*, 13, *Eberthella*, 11, *Shigella*, 3, *Alkaligenes*, 2. Other gram negative bacteria isolated were *Bacillus pyocyaneus*, 2, *Friedlaender's bacillus*, 1, *Bacillus prodigiosus*, 1.

The *Proteus* group was predominantly in the dirty wounds, 10 of the 13 isolations being in this group. The *Eberthella* group was predominant in the "clean" group, 7 of the 11 cases.

The organisms isolated in association with the gram negative bacilli were *Staphylococcus albus*, 40 times, *Staphylococcus aureus*, 11 times, hemolytic streptococci, 4 times, nonhemolytic streptococci, 10 times, *Bacillus subtilis* group, 24 times, clostridia, 10 times, micrococci, 7 times, diphtheroids, 4 times.

Anaerobic gram negative bacteria are rare, 3 cultures only having been obtained. They were *Bacterioides fragilis* from a finger wound, *Colibacterium molniformis* from a wrist wound, and *Bacterioides tenuis* from a scalp wound. *Staphylococcus aureus* infection developed in the wrist wound.

The saprophytic organisms isolated include the gram positive aerobic spore-bearing bacilli, 77 times, 41 6 per cent of the cases, the micrococci, 46 times, 25 per cent of the cases, and the gram negative cocci, 3 times, 1 6 per cent. Molds were relatively infrequent, found in 9 wounds, 4 5 per cent of the cases.

## SUMMARY

Accidental wounds are always found to be contaminated no matter how early they are seen after injury. In 200 fresh, previously untreated traumatic wounds cultures of débrided tissue showed bacteria present in every case. The types of wounds included lacerations, bullet dog and human bite, and other puncture wounds machine and automobile accidents traumatic amputations and compound fractures. Contamination occurs usually with pathogenic and often with virulent organisms. Dirty wounds are apt to show hemolytic streptococci and the gas gangrene producing anaerobic bacilli more frequently than clean wounds. However even clean-looking wounds may harbor these organisms with sufficient frequency to suspect their presence in every case. No one can tell which of these wounds is going to develop infection.

The important bacteriological findings in 200 cases are as follows: Staphylococcus aureus, 104 times, 52 per cent hemolytic streptococcus 34 times 17 per cent nonhemolytic streptococcus, 53 times 26.5 per cent green streptococcus, 18 times, 9 per cent clostridia, 46 times, 23 per cent enterobacteria, 46 times, 23 per cent and the anaerobic gram negative bacilli 3 times, 1.5 per cent. These organisms were rarely found in pure culture. (In many instances 1 or more pathogens were cultivated from the same wound.) Saprophytes, the gram positive aerobic spore bearing bacilli and gram positive cocci, were frequently seen. An average of 3 different organisms was isolated from each wound. The older the untreated wound the more commonly were anaerobes cultivated.

The knowledge of the bacterial flora in any given contaminated wound gives a sound basis for the rational prophylactic treatment to be instituted to prevent infection in that wound.

NOTE: The characteristics of the staphylococci in 33 of the 200 cases are studied. Fifty-one different colonies are

isolated in pure culture. Of these 30 are orange pigmented (aureus) and one hits (albus) variety. Thirty colonies are hemolytic on sheep's blood agar plates. All are pigmented (aureus). Nine of the pigmented strains are nonhemolytic.

Fresh isolated isolated human plasma and 4 hour dextrose broth cultures are employed in testing for coagulase. The development of firm coagulase after 4 hours incubation at 37 degrees C. as indicator of the presence of coagulase. Fourteen strains (8 cases) are coagulase positive. All these are hemolytic and pigmented. Sixteen hemolytic pigmented strains are coagulase negative and nonhemolytic strains are also coagulase negative. The latter include the nonpigmented albus strains.

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## BIBLIOGRAPHY

1. B. R. A. J. H. Clear liquid mediums for the "aerobic" cultivation of anaerobes. J. Am. M. Ass. 1920, 5, 508.
2. Dörner, A. and Gertmann, H. Zur Bakteriologie akzidenteller Wunden. Arch. f. klin. Chir. 1922, 174, 629-637.
3. Index Catalogue of the Library of the Surgeon General's Office, Third Series, vol. 2, p. 134.
4. LAURITZEN, R. C. The antitoxin complex of Streptococcus hemolyticus L. Demonstration of type specific substance in extracts of Streptococcus hemolyticus. J. Exper. Med. 1924, 47, 9.
5. LEVADITI, C. Mlle. GARLAND-MONROU, etc. B. 1907. II and TOUTY, R. Bacterial flora of traumatismes. Bull. Acad. de med. Paris, 1936, 22, 371-38.
6. MASON, M. L. Wound healing. Surg. Gynec. & Obst. 1930, 60, 303-35.
7. M. J. TOME, J. and FILPER, P. A new apparatus for the isolation and cultivation of anaerobic microorganisms. Lancet, 1916, 766-770.
8. PULASKI, E. J. and SCHWARTZ, W. R. The characteristics of staphylococci isolated from acute traumatic wounds. (To be published).
9. RATHKE, L. Bakteriologische Wunduntersuchungen. Beitrag zur Frage der Tetanus prophylaxe. Zentralbl. f. Chir. 1920, 67, 755-762.
10. RIGOLD, H. Ueber den Keimgehalt akzidenteller Wunden. Deutsche Zeitschr. f. Chir., 1909, 47, 13-64.
11. SAN, L. Beiträge zur Bakteriologie der akzidentellen Wunden. Arch. f. klin. Chir. 1920, 174, 613.
12. SYMINGTON, K. Bacterial flora of wounds before and after debridement and epilation. Soviet. Khir. 1930, 41-54.
13. V. RABIT, B. J. G. and DE VITA, J. B. Wie sieht man den aseptischen Verlauf der akzidentellen Wunden. Zentralbl. f. Chir. 1920, 67, 553-570.
14. ZIMMER, J. and NALLA, K. Anaerobic Wundinfektion im Frieden. Arch. f. klin. Chir. 1924, 40, 72.

# SULFATHIAZOLE AND SODIUM SULFATHIAZOLE IN THE TREATMENT OF POSTOPERATIVE PNEUMONIA

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IT is generally recognized that postoperative pulmonary complications are frequently encountered. The purpose of this communication is to present the results of therapy with sulfathiazole in a group of patients having postoperative pneumonia. Since "postoperative pneumonia" is a term that is often used quite loosely, it is first necessary to clarify its meaning. One of the most significant contributions made to this subject was that of Whipple in 1918. Using the term, "postoperative pneumonitis," he called attention to a little recognized but common form of postoperative pulmonary complication. This type occurred in the first 24 to 48 hours after operation, and its features were a rise in temperature, cough, increased respiratory rate, chest pain, and dullness over a portion of the lower lobes. Within a few days the symptoms subsided, the temperature declined by lysis, but the physical signs of consolidation persisted for a longer period of time. Pneumococci of the higher types were frequently isolated from the sputum of these patients. The mortality rate was low. In the light of subsequent studies by others, it is probable that the patients observed by Whipple had some degree of atelectasis associated with a low-grade pulmonary infection.

The careful clinical observations of King recorded more recently have given added information concerning the nature of postoperative pulmonary complications. He was particularly interested in those patients who, within 3 to 4 days after operation, developed fever, leucocytosis, cough, and purulent sputum. The types of pulmonary complications that these patients had could be divided into three main groups. The first were those with bronchopneumonia. The second group comprised patients having a massive collapse due

to an occlusion of a bronchus by exudate. The largest number of cases fell into the third group, and included patients having a purulent bronchitis with a low-grade bronchopneumonia (pneumonitis), sometimes in association with atelectasis due to occlusion of bronchi by exudate. King emphasized that a purulent bronchitis was the basic lesion in this third group of cases. Irons and Apfelbach have lately called attention to the pathogenesis of so called aspiration pneumonia. While the term has been frequently employed by clinicians for many years, the precise nature of the condition has not been carefully studied. Irons and Apfelbach assert that a characteristic type of pneumonia results from the aspiration of stomach contents during operation or shortly thereafter. Its features are hemorrhage, hyperemia, edema, and advanced post-mortem and retrogressive changes in the lungs. In acute cases, the bacterial flora of the stomach, lung, and bronchi are almost the same. The condition has been reproduced in dogs by the intratracheal introduction of stomach contents.

It is apparent that the pathogenesis of postoperative pneumonia is dependent upon several factors. Whipple has summarized some of the predisposing factors as follows: recent or concurrent inflammation of a part of the upper respiratory tract, pulmonary congestion, inhibition of normal respiratory movements or excursions as a result of abdominal incision, and debilitated states, such as sepsis and cachexia. Other important factors are the increased frequency of upper respiratory infections occurring during the winter and spring months, and a rise in the carrier rate of virulent pneumococci among the general population. The rôle of pulmonary congestion in the evolution of postoperative pneumonia must be stressed, because of its significance and because, in many instances, it can be prevented.

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Since pneumococci of the higher types are frequently found in the nasopharynx of normal individuals, under certain operative and postoperative conditions, these organisms may pass into the lower respiratory tract and cause an inflammatory reaction in the congested pulmonary tissue. Contributing factors are a diminution of the respiratory excursions and the cough reflex. Agencies responsible for pulmonary congestion in patients are the administration of excessive amounts of sodium chloride, and unreasonable quantities of fluids given intravenously both associated with cardiac failure.

Our clinical experience at the University Hospital has been similar to that expressed by King. We have found it very difficult to differentiate pneumonitis from atelectasis. This problem can be approached only on the basis of physical and x ray findings. Recognizing that a purulent bronchitis is the underlying lesion of both conditions, the physical findings of pneumonitis include dullness, increased tactile fremitus, increased bronchial breathing and whispered voice, and fine crackling rales. An x ray film of the chest may or may not reveal an increased area of density. If a bronchus becomes occluded by exudate the findings are those of atelectasis which are dullness, decreased tactile fremitus, and decreased breath sounds and whispered voice. X ray findings of considerable aid reveal an elevation of the diaphragm of the affected side, an increased area of density and in some instances, a shift of the mediastinum. However confusion arises many times because atelectasis may occur and then the bronchial exudate is coughed up without a simultaneous expansion of the collapsed lung. In this event there is the free passage of air into an area of atelectasis, and the physical findings closely approximate those of pneumonitis. Even an x ray film may not be helpful in the differentiation because the diaphragm may be elevated in both instances following an abdominal operation. Although King found that only about one-half of his cases of pneumonitis were accompanied by a demonstrable atelectasis, we have been unable to make a differentiation of our cases with the same degree of accuracy.

In summary then postoperative pneumonia is not a specific clinical entity. It may include patients having a typical lobar or lobular type of consolidation due, in most instances, to the pneumococcus. The mortality rate in this group of cases is high. The most common form involves those patients having a purulent bronchitis, which results in a low-grade type of pulmonary inflammation known as pneumonitis, or in atelectasis. A number of patients may have both atelectasis and pneumonitis. Considerable difficulty attends the differentiation of these two types. Finally there is a type described by Irons and Apfelbach called aspiration pneumonia.

We have endeavored to clarify the present status of the pathogenesis of postoperative pneumonia because of its direct bearing on the problem of therapy. It is not an easy task for the medical consultant to decide clinically whether he is being confronted with a patient who has a relatively benign lesion such as pneumonitis and/or atelectasis or who has the early manifestations of a lobar or lobular type of pneumococcal consolidation. Further more what may appear to be a benign process may progress to frank areas of consolidation and endanger the life of the patient. Therefore, for the protection of the patient every thing in the form of treatment should be carried out, and specific therapy if available should be instituted without delay.

Pneumococci of the higher types are usually found in the sputa of patients with postoperative pneumonia. It is clearly recognized that these micro-organisms are often normal inhabitants of the nasopharynx and may have no etiological relationship with the pulmonary lesion. But when they are consistently encountered in large numbers in sputum, it may be reasonably assumed that there is a correlation. The problem is easily resolved when the more virulent pneumococci of lower types are present. It is only within the past few years that specific therapeutic agents have been available for use against the higher types of pneumococci. Type-specific antipneumococcal rabbit sera have been successfully employed. We have always been reluctant to use rabbit serum for these patients because of the danger of reactions in a seriously ill patient, and be

cause, in the majority of patients, the pulmonary infection has been relatively benign. The recent advances in chemotherapy have permitted a more successful application of specific agents in the treatment of all types of postoperative pulmonary infections, particularly those due to the pneumococci. While sulfapyridine has been used widely in the treatment of pneumonia, little data have been recorded in the literature concerning its value in the therapy of postoperative pneumonia. Hinshaw and Moersch administered sulfapyridine orally in 21 cases of postoperative pneumonia, and the patients responded as well as those with primary pneumonia. It is significant that half of the number of patients treated by them became nauseated because of the drug, and it was necessary to shorten the duration of sulfapyridine therapy in a number of others because of vomiting. We have had corresponding results in the treatment of many patients with postoperative pneumonia. In patients who were unable to take the drug by mouth, a solution of the sodium salt of sulfapyridine was administered intravenously with equally satisfactory results. However, when using sulfapyridine, one is constantly apprehensive concerning the harmful effect of the nausea and vomiting upon the operative wound of the patient as well as the added discomfort involved.

Sulfathiazole is a compound that has been used more recently in the treatment of pneumococcal pneumonia. Experimental and clinical data (1, 5, 6, 7, 9, 10) indicate that sulfathiazole is at least as effective as sulfapyridine upon the pneumococcus. During the past 6 months, we have used sulfathiazole and its sodium salt in the treatment of 40 patients with primary pneumococcal pneumonia, and the clinical results were equally as good as those obtained with sulfapyridine. Sulfathiazole had the added advantage in that it was followed much less frequently by nausea and vomiting. This latter observation has prompted the use of sulfathiazole and sodium sulfathiazole in the treatment of postoperative pneumonia in patients on the surgical services of the University Hospitals. The results have been highly satisfactory, and we desire to present observations that have been made

#### MATERIAL AND METHODS

A total of 22 patients was treated, including 15 males and 7 females. In all of the patients, clinical findings were elicited which fulfilled the criteria for a diagnosis of postoperative pneumonia. The patients have been divided into two groups. The first group, consisting of 6 patients, had bronchopneumonia with definite evidence of pulmonary consolidation. The 16 remaining patients had pneumonitis and atelectasis. The difficulties encountered in differentiating pneumonitis from atelectasis have already been recounted, and in the present group, we were unable to dissociate the two conditions. Therefore, we have classified this group as having pneumonitis and atelectasis. When available, sputa were examined bacteriologically, and typing for pneumococci was performed by the Neufeld method. Blood cultures were obtained before the institution of therapy with sulfathiazole.<sup>1</sup> An x-ray film of the chest was made as soon as the diagnosis of a pulmonary complication was considered. Bronchoscopy was performed upon one patient by Dr. Logan Leven in an attempt to remove an occluding plug of exudate from a bronchus. Sulfathiazole tablets were administered orally whenever possible. The initial dose was 2 to 4 grams, and then 1 gram every 4 hours for approximately 5 days. When the drug was given for a longer period, the doses were reduced. Sodium bicarbonate was administered along with sulfathiazole to only 4 patients. It appears very doubtful whether it is necessary to use the alkali in conjunction with sulfathiazole. There were 12 patients who were unable to take any medication orally, and a solution of the sodium salt of sulfathiazole was given intravenously. A 5 per cent solution in warm sterile distilled water was used. The initial dose was 2 to 3 grams (40 to 60 c cm) and then 1 gram (20 c cm) every 8 hours. As soon as possible, 1 gram of the sulfathiazole tablets was given orally every 4 hours. The concentrations of both the free and conjugated forms in the blood were determined by the method of Bratton and Marshall, using the Evelyn

<sup>1</sup>The bacteriological studies were performed by Dr. M. V. Novak and Dr. M. Levine of the Bacteriological Laboratories of the University Hospitals.



TABLE I—POSTOPERATIVE BRONCHOPNEUMONIA TREATED WITH SULFATHIAZOLE

| Case No.<br>Sex | Operation                                     | Site of<br>pulmonary<br>lesion* | Postopera-<br>tive<br>interval | Pneumo-<br>coccus<br>type | Sulfathiazole therapy            |                      |   |                 | Comment                           |   |
|-----------------|---|---------------------------------|--------------------------------|---------------------------|----------------------------------|----------------------|---|-----------------|-----------------------------------|---|
|                 |   |                                 |                                |                           | Total dose<br>(grams)            | Days of<br>treatment | Blood level   |                 |                                   | Toxic<br>reactions                                |
|                 |   |                                 |                                |                           |                                  |                      | Free  | Con-<br>jugated |                                   |   |
|                 |   |                                 |                                |                           |                                  | (mgm./<br>100 cc.)   |   |                 |                                   |   |
| 11<br>M         | Excision of pancreatic adenoma                | R.L.L.                          | 24 hrs.                        | atol.                     | 36                               | 7                    | 3.5   | 3.8             | None                              | Recovery  |
| 14<br>F         | Excision of spinal cord tumor                 | R.L.L.<br>L.L.L.                | 24 hrs.                        | —                         | 36                               | 8                    | 4   | 1.6             | None                              | Recovery; spinal<br>effusion—sterile              |
| 3<br>M          | Axillary dissection (osteosarcoma metastasis) | R.L.L.                          | hrs.                           | 13                        | 40                               |                      |   |                 | None                              | Slight increase of<br>hem. leucocytes<br>recovery |
| 11<br>M         | Appendectomy                                  | L.L.L.                          | 22 hrs.                        | 19                        | 25                               | 6                    |   |                 | Slight<br>nausea                  | Recovery  |
| 7<br>F          | Colestomy (volvulus of cecum)                 | R.L.L.                          | hrs.                           | —                         | 750<br>Sulfathiazole<br>12.5 gm. |                      |   | 9.3             | Slight<br>nausea,<br>loose stools | Recovery  |
| 6<br>F          | Gastrectomy                                   | L.L.L.                          | hrs.                           | 19                        | 750<br>Sulfathiazole<br>20 gm.   | 8                    | 21.8<br>(24 hrs.<br>after second<br>dose)<br>20.0<br>(24 hrs.<br>after first<br>dose) |                 | None                              | Recovery  |

\*R.L.L. right lower lobe; L.L.L. left lower lobe.

photoelectric colorimeter. Careful observations were made for toxic reactions to the drug.<sup>1</sup>

### RESULTS

Pertinent clinical data concerning the patients having bronchopneumonia are shown in Table I. All of the patients recovered. Pneumococci were not recovered from the blood streams of any of the patients in either group. Following the administration of sulfathiazole, the fever subsided and there was definite clinical improvement within 24 hours. A solution of sodium sulfathiazole was given intravenously to 3 of the 6 patients. It is of interest to note the concentrations of sulfathiazole attained in Case 6. Twenty minutes after 3 grams of sodium sulfathiazole had been given

the blood level of free sulfathiazole was 24.8 milligrams per 100 cubic centimeters. There were 1.3 milligrams present as the conjugated form. Twelve hours later 1 gram of the salt was administered and twenty minutes later the blood concentration of free sulfathiazole was 15.2 milligrams per 100 cubic centimeters and the level of the conjugated form was 1 milligram.

The results in the larger group of patients having pneumonitis and atelectasis are presented in Table II. The clinical response in this group was also quite definite coincident with the administration of sulfathiazole. There was a decline in temperature and in none of the patients was there a progression of the pulmonary lesion. Two patients in this group expired from complications unrelated to their pulmonary infections or sulfathiazole therapy. Ten of the patients received the sodium salt intravenously. One patient (Case 5) had been given a total of 5 grams of sulfapyridine by mouth following which she experienced an episode of severe vomiting. When the vomit

\*Here severely we have treated groups of patients by administering solution of sodium sulfathiazole subcutaneously. Disregarding even the seriousness of the patient, almost from 5 to 10 cc. of the sodium salt are dissolved in 100 cc. of physiological saline solution (i. e. 1 per cent concentration of sodium sulfathiazole). This gives by hypodermoclysis at the rate of about 100 to 200 cubic centimeters per hour. The concentration of sodium sulfathiazole is not irritating to the tissue. In this manner an adequate blood concentration of sulfathiazole can be maintained for 24 hours or more. T. Wilson, observed blood concentrations of sulfathiazole quickly to those of sodium sulfathiazole are given intravenously at the same time the subcutaneous concentration started.

TABLE II—POSTOPERATIVE PNEUMONITIS AND ATELECTASIS TREATED WITH SULFATHIAZOLE

| Case<br>Age<br>Sex | Operation  | Site of<br>pulmonary<br>lesion* | Postoper-<br>ative<br>interval | Pneumo-<br>coccus<br>type | Sulfathiazole therapy                            |                      |                   |                 |                           | Comment   |
|--------------------|--|---------------------------------|--------------------------------|---------------------------|--|----------------------|-------------------|-----------------|---------------------------|---|
|                    |  |                                 |                                |                           | Total dose<br>(grams)                            | Days of<br>treatment | Blood level       |                 | Toxic<br>reactions        |   |
|                    |  |                                 |                                |                           |  |                      | Free              | Con-<br>jugated |                           |   |
|                    |  |                                 |                                |                           |  |                      |                   |                 |                           |   |
| 7<br>26<br>F       | Cholecystectomy  | RLL<br>RML                      | 6 hrs                          | xx xix<br>xxix            | 4 gm<br>sodium<br>18 0 total                     | 4                    | 3 6               | 8               | None                      | Recovery  |
| 8<br>20<br>F       | Splenectomy (leucopenia)   | RLL                             | 24 hrs                         | xix xi                    | 12<br>8  | 2<br>2               | 2 4<br>1 6        | 4<br>8          | Nausea                    | Recovery 2 attacks<br>—one 24 hrs<br>postoperative<br>2d 7 days post<br>operative<br>Bronchoscopy 1st<br>attack |
| 9<br>70<br>F       | Cholecystectomy  | RLL<br>LLL                      | 48 hrs                         | —                         | 2 gm<br>sodium                                   | 1                    | 3 2               | 6               | None                      | Recovery after<br>5 gm sulfa<br>pyridine severe<br>vomiting   |
| 10<br>27<br>M      | Plastic craniotomy   | RLL                             | 6 days                         | xxxi                      | 38   | 7                    | 4 3               | 3               | None                      | Recovery  |
| 11<br>40<br>M      | Gastric resection  | RLL<br>LLL                      | 7 hrs                          | iv                        | 11 gm<br>sodium                                  | 5                    | 6 5<br>3 1        | 2 0<br>1 1      | None                      | Recovery  |
| 12<br>68<br>M      | Colostomy (intestinal obstruction<br>Fractured femur)                  | RLL<br>LLL                      | 5 hrs                          | —                         | 6 gm<br>sodium<br>in 2 doses<br>4 gm and<br>2 gm | 6                    |                   |                 | None                      | E. coli bacteremia<br>Epididymitis<br>Died  |
| 13<br>53<br>M      | Gastric resection  | LLL                             | 24 hrs                         | vi                        | 8 gm<br>sodium<br>13 0 total                     | 5                    | 2 0<br>1 3<br>2 6 | 1 0<br>8<br>1 0 | None                      | Recovery  |
| 14<br>66<br>M      | Perforated gall bladder<br>cholecystectomy                             | RLL<br>LLL                      | 24 hrs                         | —                         | 6 gm<br>sodium                                   | 2                    | 1 6               | 4               | None                      | Recovery  |
| 15<br>41<br>M      | Appendectomy cholecystectomy<br>choledocholithotomy<br>choledochostomy | RLL                             | 36 hrs                         | xi                        | 3 gm<br>sodium<br>33 0 total                     | 7                    | 1 4<br>4 8<br>4 2 | 2<br>8<br>1 0   | None                      | Recovery  |
| 16<br>21<br>M      | Appendectomy   | LLL                             | 5 hrs                          | xxii                      | 6 gm<br>sodium<br>21 0 total                     | 5                    | 4 2               | 5               | None                      | Recovery  |
| 17<br>66<br>F      | Gastric resection  | RLL<br>LLL                      | 7 hrs                          | xv                        | 8 gm<br>sodium                                   | 3                    | 5 6               | 1 2             | None                      | Recovery  |
| 18<br>35<br>M      | Intervertebral discectomy  | RLL                             | 6 hrs                          | xxiv                      | 37   | 7                    | 5 9<br>5 1        | 2<br>6          | None                      | Recovery  |
| 19<br>10<br>F      | Nephrostomy pelvolithotomy<br>Inc abscess thigh                        | RLL                             | 48 hrs                         | —                         | 43   | 8                    | 3 2<br>5 7        | 4<br>1 0        | Nausea<br>derma-<br>titis | Recovery Rash<br>on eighth day  |
| 20<br>44<br>M      | Gastric resection  | RLL                             | 6 hrs                          | —                         | 16 gm<br>sodium                                  | 6                    | 2 4<br>4 7        | 8<br>3          | None                      | Recovery  |
| 21<br>57<br>M      | Appendectomy   | RLL                             | 12 hrs                         | xv                        | 8  | 5                    | 1 2<br>1 4        | 2<br>1 0        | None                      | Evisceration<br>Died  |
| 22<br>55<br>M      | Appendectomy cholecystectomy   | RLL                             | 12 hrs                         | —                         | 52   | 14                   | 9 8<br>9 8<br>1   | 2 0<br>3 7<br>9 | None                      | Recovery  |

\*RLL right lower lobe.

LLL left lower lobe

RML right middle lobe

ing had subsided sodium sulfathiazole was given intravenously with no untoward effects.

It is difficult to state at the present time what is the desirable blood concentration of sulfathiazole for the treatment of patients with postoperative pneumonia. Satisfactory clinical results were obtained in the present series with levels of free sulfathiazole from 3 to 5 milligrams per 100 cubic centimeters of blood.

The toxic manifestations from sulfathiazole were less than those encountered following the use of sulfapyridine. Smaller amounts of the circulating sulfathiazole were present as the conjugated form as compared to sulfapyridine. Four of the patients complained of nausea during the course of treatment, but in none was it severe enough to necessitate withdrawal of the drug. One patient developed a gross hematuria without other evidence of impaired renal function. In 1 individual an erythema nodosum-like eruption appeared on the extremities after 8 days of sulfathiazole. The lesions subsided when sulfathiazole therapy was stopped.

#### VALUE OF SULFATHIAZOLE THERAPY

We do not desire to imply that the recovery of the patients in this series was due entirely to the use of sulfathiazole. Conclusions concerning the therapeutic effectiveness of the drug can be based only upon the results obtained in a much larger series of cases. The important point that we wish to make is since it is often exceedingly difficult to make a clinical distinction between an early lobar or lobular pneumonia and pneumonitis and/or atelectasis in an acutely ill patient, sulfathiazole is a specific antipneumococcal agent that may be given with a reasonable degree of safety. At the present time, we do not hesitate to administer the drug to any patient with a relatively benign pulmonary infection but in whom a number of other factors have reduced his resistance so that a progression of the lesion would tip the balance against his recovery. Sulfathiazole is of especial value in the therapy of postoperative pneumonia in that it may be readily administered intravenously in the form of sodium sulfathiazole.

#### SUMMARY

1 The term postoperative pneumonia is applied to patients having a lobular or lobar type of consolidation, or a purulent bronchitis with a low-grade type of parenchymal inflammation usually accompanied by atelectasis. The pneumococcus is the etiological agent in the majority of cases.

2 Twenty-two patients with postoperative pneumonia were treated with sulfathiazole and/or sodium sulfathiazole with satisfactory clinical results.

3 Since sulfathiazole causes less nausea and vomiting and appears to be equally as effective for pneumococcal pulmonary infections as sulfapyridine it is recommended that sulfathiazole or sodium sulfathiazole should be used in the treatment of postoperative pneumonia.

#### BIBLIOGRAPHY

- BRATTON, A. C., and MARSHALL, E. K., JR. A new coupling component for sulfanilamide determination. *J Biol Chem.* 1939 125 377.
- FLETCHER, H. F., SCHWARTZ, L., and KONE, S. B. The comparative effectiveness and toxicity of sulfathiazole and sulfapyridine in pneumococcal pneumonia. *Ann. Int. Med.* 1940, 3 2938.
- FRIDLAND, H. C., and MOSKOWITZ, H. J. Sulfapyridine in treatment of pneumonia, its special reference to postoperative pneumonia. *Arch. Surg.* 1939, 74 275.
- FEIGER, E. E., and ARFELSON, C. W. Application pneumonia; its special reference to aspiration of stomach contents. *J. Am. M. Ass.* 1940, 3 584.
- KRIV, D. S. Postoperative pulmonary complications: I. A statistical study based on 10 years' personal observations. *Surg., Gynec. & Obst.* 1935, 58 43.
- LAURENCE, C. A. Bacteriostatic actions of three thiazol derivatives of sulfanilamide upon bacteria in broth cultures. *Proc. Soc. Exper. Biol. & Med.* 1940, 43 9.
- LONG, P. H. Thiazole derivatives of sulfanilamide. Sulfathiazole and sulfamethylthiazole. *J. Am. M. Ass.* 1940, 4 870.
- LONG, P. H., and BUISE, E. A. Bacteriostatic effects of sulfathiazole upon various microorganisms. Its therapeutic effects in experimental pneumococcal infections. *Proc. Soc. Exper. Biol. & Med.* 1940, 43 324.
- McKAY, C. M., RAKE, G., GREEP, R. O., and DYER, M. B. Therapeutic effect of sulfathiazole and sulfapyridine. *Proc. Soc. Exper. Biol. & Med.* 1940, 43 47.
- SPRING, W. W., and H. YOUNG, A. E. Sulfathiazole clinical evaluation. *J. Am. M. Ass.* 1940, 3 890.
- WATKINS, A. O. A study of postoperative pneumonia. *Surg. Gynec. & Obst.* 1940, 30 29.

# SULFONE CHEMOTHERAPY IN HEMATOGENOUS OSTEOMYELITIS

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THE prognosis of any single case of acute osteomyelitis depends on many variable factors. Some of these, such as the time and extent of operation, and the type of after-care, can to a great extent be controlled by the surgeon, others, such as the strain and virulence of invading organisms, the previous medical condition of the patient, his powers of resistance, and the intensity of the local tissue reaction, are altogether beyond his control. Therefore, in considering the effect of any procedure on the course of the disease, one must attempt to evaluate that procedure by reasonably simple and tangible criteria. With this premise in mind, 20 cases of hematogenous osteomyelitis were reviewed in which chemotherapy with sulfone derivatives was used as part of the treatment. Aside from the use of these drugs, the patients were treated no differently than were other patients with similar conditions before the introduction of the drugs or, in a number of instances, concurrently. From time to time different types of bone excision have been used, such as drill holes, cortical windows or bone wedges, but in all instances the general approach of establishing adequate drainage at the optimal time, followed by the Orr treatment or a modification thereof to suit the individual case, was carried out.

The present series while not large represents 3 years of experience with carefully studied cases. During this period the drugs have been used on many more cases, such as secondarily infected wounds, which were not included in the investigation. To the writer's knowledge, no comparable series has as yet been reported. Mitchell, in 1938, published his results in 5 cases of *Staphylococcus aureus* osteomyelitis treated by uleron (Bayer's sulfanilamide), Weidekamp, in the same year, discussed the use of prontosil in tuberculous and non-tuberculous osteomyelitis, including 1 case

of the latter. Many of the recent papers which review the general subject of the clinical use of sulfone derivatives, mention their application to osteomyelitis without discussing their effect on the course of the disease other than the control of general sepsis.

The effect of sulfone chemotherapy on general sepsis in streptococcus and staphylococcus infections is being adequately studied by many investigators and its present value is fairly well established. Likewise the pathology and general course of osteomyelitis has been thoroughly described by Lexer, Wilensky (9), Key, Phemister, Brown, and many others, and also requires no further discussion at this time. For present purposes the objective has been limited to a study of the effect of sulfone chemotherapy added to standard surgical procedures on (1) the course of the local bone pathological process, (2) on recurrence, and (3) on metastases. It is common knowledge among those who have watched the natural course of the disease that the establishment of drainage, even early in the disease, does not necessarily prevent the progressive involvement of bone over a more or less limited area of the adjacent shaft. This is easily demonstrated by a series of x-ray films taken during the postoperative period. In successful cases, this area gradually regains its normal appearance. In widespread lesions, the reorganization of bone structure in healed cases may not be completely normal in structure, but still consists of well established trabeculae and canals. If the addition of sulfone medication to the treatment could be shown either to eliminate or significantly retard this cycle of postoperative necrosis in a large percentage of cases, then its effect on the local infection would be demonstrated. If cases so treated showed a considerable decrease in recurrences or in metastases, its value would be evident. The cases in this series were analyzed with these criteria in mind.

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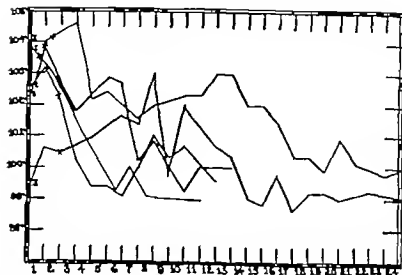


Chart 1. Temperature levels.  $\times$  start of use of drug I II III sulfanilamide  
 & sulfapyridine

In the earlier cases of this series, as in Mitchell's cases, sulfanilamide was used for both staphylococcal and streptococcal infections. As the derivative sulfapyridine and later sulfathiazole appeared, these were used on staphylococcal cases, and sulfanilamide was reserved for the beta hemolytic streptococcus. In several instances combinations running either simultaneously or in sequence were used. In general it may be stated here that in the earlier cases in which sulfanilamide was used in staphylococcal osteomyelitis, patients recovered in a manner very similar to that of later cases. There was the same drop in temperature, the same cycle of bone involvement, and the same general recovery. These cases resembled those reported by Mitchell. The present series shows the usual variety of age, duration, location, operative time, and other factors as would be found in any current or preceding series. In discussing these cases, the significant facts will be mentioned at some length. The corroborating details can be studied only by examining the data of the individual cases summarized.

#### EFFECT ON TEMPERATURE

One of the dramatic manifestations of the use of sulfone derivatives in the various infec-

tions has been the sudden drop in temperature which frequently follows. This is especially remarkable in such infections as pneumonia, streptococcal sore throat, and meningitis. Chart 1 shows a composite picture of 6 characteristic temperature charts. Reference to similar charts published by Wilensky (10) on patients treated without sulfone medication, and confirmed by our own charts in similar cases, demonstrates no significant alteration. In most instances, following the establishment of drainage in uncomplicated cases, the temperature does drop from a relatively high level to a lower. Occasionally the drop is to normal in a few days; usually it falls to between 100-101 degrees and gradually subsides to normal in a week or two in the less extensive infections, or in a longer period in the more widespread cases. In the present series, the temperature readings did not as a group deviate from groups in which sulfone chemotherapy was not used. The temperature readings varied with the local infection and its surgical aspects, that is, drainage, area of infection, and intensity of tissue reaction. In several streptococcal cases in which patients were not operated upon, the temperature fell soon after the application of a plaster-of-Paris bandage and the customary dose of sulfanilamide given

by mouth, but not more rapidly than has occurred in similar cases in which patients were treated only by plaster

#### WOUND HEALING TIME

The length of time of healing of the operative wound in these cases was not noticeably shortened. Here again it varied with the customary rules of surgical practice, that is, the extent of wound surface, and persistence of drainage. There was no noticeable difference in the quality or quantity of granulation tissue.

#### BONE NECROSIS

This phenomenon was studied in some detail. Figures 1 to 3 show characteristic cycles in several of the cases which were adequately drained at an optimal time. The patients were relieved after operation and by all the customary objective and subjective observations went through the usual course of an uneventful recovery from acute hematogenous osteomyelitis. Sulfone therapy did not to any measurable degree retard or restrain the completion of the cycle of bone absorption and restoration in these cases. There were 7 such cases in the present series. A number of cases, especially in the younger age group, recovered without bone changes, after simple incision of subperiosteal abscesses. These cases followed the course and time elements of such patients treated similarly without sulfone chemotherapy.

#### RECURRENCES

Recurrence in this study refers to local reactivation of a clinically healed lesion as distinct from an exacerbation of an unhealed area, or the late appearance of a metastatic focus. In this series there have already been two recurrences, both in staphylococcal infections. In neither case was the recurrence operated upon. In one instance it subsided in a week with wet dressings and sulfapyridine, in the other, wet dressings were enough. The latter was, on his first admission for sulfone therapy, an acute recurrence of an old osteomyelitis. The infection was not eradicated by the drug.

#### METASTASES

Metastatic foci were observed during the period of treatment or soon thereafter in 2

cases. Here again the percentage is about the same as in larger series treated without sulfone derivatives. In one very active staphylococcal infection, with severe septicemia, involving primarily the clavicle, there were metastases to both humeri, and the left tibia. There was also a widespread papulopustular skin eruption (3). In another staphylococcal infection of the femur, secondary foci appeared about the ankle and alveolar process.

#### TOXIC MANIFESTATIONS

In one of the earliest cases in which sulfapyridine was used the patient died of a typical agranulocytosis. The drug was given for 5 days beginning on the day of admission, which was also the day of operation. On the fifth day, temperature was normal, and the patient in excellent condition. It was decided to continue the drug in the hope of definitely eliminating the staphylococcal infection. Five days later, the white blood count was still 10,600, 2 days later it had dropped to 4,000, with 72 per cent polymorphonuclears. The drug was stopped. Next day the count was 3,400 cells, 24 per cent polymorphonuclears. Six days later, during which period daily transfusions and full doses of pentonucleotide were given, the white count fell to less than 300 cells, all of which were lymphocytes, and the patient died. In all, the patient had been given 93 grams of sulfapyridine between March 28 and April 13. This case has been reported in detail elsewhere (7). Aside from this instance there were no other serious toxic manifestations. In several cases the drug was stopped because of nausea or excessive blueness. The latter symptom is no longer dreaded as at first, but marked nausea is still taken seriously.

#### BLOOD CULTURES

In 7 cases the blood showed *Staphylococcus aureus* on culture, in 2 cases, *Streptococcus haemolyticus* appeared. In 2 cases both of these organisms appeared together, and in 9 cases the blood showed no organisms at all. In all but 1 case showing positive blood cultures, these were sterile from 2 to 5 days after the institution of treatment, regardless of the state of healing of the local infection. The only case in which the blood cultures re-

maintained positive for a considerably longer period was in the patient who suffered multiple metastases and the generalized pustular eruption.

#### ANALYSIS OF RESULTS

All the cases were treated according to standard surgical indications. The addition of sulfone chemotherapy was supplementary. Of the 3 patients not operated upon 1 showed *Streptococcus haemolyticus* in the blood stream; the blood cultures of the 2 others were negative. One case involved the pubis, another the edge of the astragalus, and the third was an acute recurrence of an old osteomyelitis of the femur without sequestrum. All 3 of these patients would have been handled similarly even without chemotherapy and compared to similar cases the condition might well have subsided without operation. Whether the outcome was influenced by the sulfone therapy, employed is conjectural, but the length of time involved in their resolution as compared to that in similar cases in which patients were treated conservatively without the use of such drugs was not markedly altered. In uncomplicated cases in which the condition subsided shortly after operation, no treatment was used other than surgical after care. In cases in which the infection did not subside promptly blood transfusions were given freely. In several severe cases of staphylococcemia, along with sulfone therapy, staphylococcal antitoxin was used in large amounts. It must be noted that had these infections responded to the drug, the prolonged use of additional forms of therapy would not have been indicated.

However, it is necessary to remark on certain phases of sulfone therapy in connection with this problem in order not to present a too one-sided observation. Unquestionably the instances of acute osteomyelitis following ear, nose and throat infections have been decreased since the sulfone drugs have been used in their treatment. Furthermore, those patients whose local lesions do not subside promptly after operation do not present the characteristic general septic appearance that was so often seen in past years. The bacteremia can unquestionably be controlled during this period. However, it must be

noted, that, after the drug is stopped, the local focus, if it persists, can still be the source of metastases. Furthermore, it cannot be disproved that certain of the metastases occurred even during the time the drug was used. Temperature levels are kept at a lower plane during the acute febrile state when sulfone therapy is used. It is important to recognize this fact to avoid neglecting still undrained areas. In several instances, a temperature level would rise during a period when the drug was withheld, and fall to a lower level when it was again used, thus indicating a specific antipyretic action.

#### SUMMARY OF CASE HISTORIES

**CASE 1:** Male, aged 7 years, was admitted to the hospital February 3, 1930, because of pain near the left ankle, of 6 days' duration. Wet dressings were applied. From February 1 to 3, 1 to 6 grams of sulfanilamide were given. On February 13, subperiosteal abscess over the lower end of the tibia, as incised and packed with vasoline gauze. On February 15, 370 cubic centimeters whole blood transfusion was given. Blood culture on February 13 showed *Staphylococcus aureus*. February 14, hemoglobin was 58 per cent; red blood cells numbered 3,650,000; white blood cells, 3,300. February 16, hemoglobin was 7 per cent. March 6, hemoglobin was 76 per cent; red blood cells, 4,470,000; white blood cells, 9,300.

Patient was readmitted on March 6, 1930, at which time there was a recurrence of tenderness and swelling at the ankle. The wound had healed. Temperature was 1 degree but subsided with the administration of wet dressings and the administration of sulfapyridine (1 gram) was given from March 8 to 9.

**CASE 2:** Male, aged 1 year, as admitted to the hospital February 3, 1930, with pain in the right knee for 4 days. He had fever. X-rays films showed early cortical bone lesion of the metaphysis of the tibia. On February 5, subperiosteal abscess as incised and packed. From February 4 to 7, 30 grams of sulfanilamide were given. On February 3, hemoglobin was 60 per cent; white blood cells, 2,700. February 17, hemoglobin was 60 per cent; white blood cells, 7,600. March, hemoglobin was 67 per cent. February 1, 500 cubic centimeter blood transfusion was given. Blood culture on February 3 showed *Staphylococcus aureus*. On February 5 it was sterile.

On March 3, patient was discharged with a draining sinus. On July 3, 1930, the wound was finally healed. During the time of treatment, serial X-ray films showed an increase in the area of bone involvement through the upper fourth of the tibia shaft, followed by gradual regeneration and increased density of bone substance.



Fig 1 Case 7 Left above, before operation, and left below and right, 2 months after operation

CASE 3 Female, aged 66 years, was admitted to hospital February 7, 1938, for pain in the upper end of the tibia, duration, 1 month. Nineteen years previously patient had been operated on for a bone abscess in this area but had remained symptom-free ever since. February 16, a cortical window was removed at the level of the lesion in the upper end of the tibia. From February 21 to 26, 10 grams of sulfanilamide were given. On March 18, a plastic closure of the wound was performed. Hemoglobin remained around 80 per cent during hospital stay. Blood culture showed *Streptococcus hemolyticus*  $\beta$ . Before discharge in April, 1938, the wound had reopened and was draining.

CASE 4 Male, aged 1½ years, was admitted to the hospital April 13, 1939, with pain in the right wrist and with fever and malaise of 1 day's duration. On April 15, a subperiosteal abscess over the lower end of the right radius was incised and packed. On April 22, the operative incision was enlarged and repacked. From April 15 to 23, 16 grams of sulfanilamide were given. From April 20 to May 6, 32 grams of sulfapyridine were given (from April 20 through the 23rd, both were given concurrently). During this time 10 transfusions of 250 to 500 cubic centimeters each were given, 300,000 units of staphylococcus antitoxin, 40 cubic centimeters of scarletinal convalescent serum, and large amounts of intravenous glucose and calcium. On April 13, white blood cells numbered 23,000, April 17, white

blood cells, 6,000, April 18, white blood cells, 4,500, with normal differential. April 28, white blood cells numbered 3,400. Blood culture showed *Staphylococcus aureus*  $\alpha$ , and *Streptococcus hemolyticus*  $\beta$ .

Patient was readmitted on August 19, 1939, with a draining sinus and rise in temperature. He was discharged with subsidence of symptoms. On March 28, 1940, the patient was readmitted because of extensive bone necrosis of the lower two-thirds of the radius. A diaphysectomy was performed and a bone transplant inserted.

CASE 5 Male, aged 9 years, was admitted to the hospital April 26, 1940, with pain in the groin, of duration of 8 days. He had fever. X-ray films showed an osteomyelitic lesion in the right pubis. From April 29 to May 2, 13 grams of sulfanilamide were given. From May 2 to 9, 27 grams of sulfathiazole were given. On April 26, hemoglobin was 75 per cent, white blood cells, 14,500, sedimentation rate, 22 minutes. Blood culture was negative. In September, 1940, x-ray films showed some localized process in the pubis with evident regeneration of bone in that area.

CASE 6 Female, aged 58 years, was admitted to the hospital on September 9, 1939, with osteomyelitis of the femur. Symptoms had been present for 3 weeks. This was an acute recurrence of an old symptom-free osteomyelitis. Wet dressings were applied, and 10 grams of sulfapyridine were given from September 9 to September 12. Wound culture showed





Fig. Case 4. Pre-operative, postoperative, and healed.

*Staphylococcus aureus* and Hemoglobin on September 9 was 94 per cent white blood cells, 8,500, with normal differential. Symptoms subsided and patient was discharged. Three weeks later there was a similar recurrence which subsided under wet dressings without the use of sulfone drugs. Patient has been symptom free ever since.

**CASE 7.** Female aged 3 years, admitted to the hospital on March 4, 1939, with osteomyelitis of the humerus duration of symptoms, 4 days. Initial x-ray films showed faint haziness about the upper metaphysis. On the day of admission, subperiosteal incision was packed with vaseline gauze after it was incised. Seventy-two grams of sulfapyridine were given from March 4 to March 7. Blood culture showed *Staphylococcus aureus* on March 5 and was negative on March 15. On March 4, the white blood cell count was 2,000 hemoglobin, 65 per cent. On March 5, the white blood cell count was 8,400 hemoglobin 6 per cent. On March 3, the white blood cell count was 8,600 hemoglobin 60 per cent. On March 8, the hemoglobin was 58 per cent, and a transfusion of 35 cubic centimeters of blood was given. Serial x-ray films taken during the stay at the hospital showed progressive destruction of the upper third of the humerus. Patient was readmitted to the hospital on November 7, 1939, with two draining sinuses. On the following day, sequesterum was removed. On April 5, 1940, the patient still presented a draining sinus. X-ray films showed increasing density of the lesion in the bone.

**CASE 8.** Female aged 3 years was admitted to the hospital on August 1, 1939, with pain in her chest 1 day duration. X-ray examination re-

vealed osteomyelitis of a rib. From August 3 to August 5, grams of sulfapyridine were given. On August 29 the bone incision was incised and packed. Wound culture showed *Staphylococcus aureus* and *Streptococcus hemolyticus*  $\beta$ . Hemoglobin on August 29 was 92 per cent white blood cells, 7,700. On August 30 hemoglobin was 84 per cent. Blood culture was negative. Ten months later the wound was still draining and the x-ray showed no change in the local lesion.

**CASE 9.** Male aged 4 years, admitted to the hospital on August 4, 1939, with osteomyelitis of the sternum duration of symptoms, 4 days. Ten-four grams of sulfapyridine were given from August 24 to August 31. On August 27 the lesion in the sternum was incised and drained. Blood culture showed *Staphylococcus aureus* and *Streptococcus hemolyticus*  $\beta$ . On August 4 the hemoglobin was 95 per cent red blood cells numbered 5,500,000 white blood cells, 20,000 sedimentation rate as 35 hours. On August 6 the white blood cell numbered 8,000. On December 4, 1939, the wound was entirely healed.

**CASE 10.** Male aged 8 years was admitted to the hospital on July 7, 1939, with osteomyelitis of the fibula duration of symptoms, 2 weeks. This was a recurrence of a lesion about 20 years previously and asymptomatic since that time. On July 18, diaphysectomy was performed. From July 9 to July 16, grams of sulfanilamide were given. Hemoglobin as maintained between 55 and 65 per cent during the hospital stay. On August 8, 500 cubic centimeter blood transfusion was given. Wound culture showed *Staphylococcus aureus*. Following the operation, the wound drained. The temperature remained at 100 degree level for over month.

**CASE 11.** Male aged 33 years, was admitted to the hospital on March 27, 1939, with pain about the hip duration of symptoms, 2 weeks. A diagnosis of osteomyelitis involving the ileum and upper end of the femur was confirmed by the x-ray on March 30. The bone lesion was incised and packed. From March 27 to April 1, grams of sulfanilamide were given. The bone incision as it further extended on April 27 because of persistent drainage. Blood culture was negative and wound culture showed *Staphylococcus aureus*. On admission the patient was acutely ill with temperature of 104 degrees F. This fell after the first operation but rose to 103 degrees F. One week later and continued to rise and fall till the second operation was performed. On March 7 hemoglobin was 7 per cent white blood cells, 9,700. On April hemoglobin was 64 per cent white blood cells 9,700. The wound as still draining at the time of discharge and there was no signs months later of bony regeneration.

**CASE 12.** Male, aged 6 years was admitted to the hospital on March 18, 1939, with osteomyelitis of the upper end of the humerus. Duration of symptoms was 3 days. On the day of admission, the bone was incised and the wound packed. Blood cul-

ture on March 28 showed *Staphylococcus aureus*  $\alpha$  and was negative on April 2. One hundred and ninety-three grams of sulfapyridine were given. On March 28, the hemoglobin was 95 per cent, white blood cells, 16,700. On March 30, white blood cells numbered 11,000. On April 5, white blood cells numbered 11,800. On April 10, the white blood cells were 10,600. On April 12, the cell count had dropped to 4,000, with 72 per cent polymorphonuclears, and on April 14 to 3,400, with 24 per cent polymorphonuclears. On April 19, the white blood cells were counted below 300 with 100 per cent lymphocytes. Beginning on April 14, blood transfusions of from 250 to 500 cubic centimeters were given daily and 10 cubic centimeters of pentonucleotide were given four times a day. Patient died on April 20, 1939.

CASE 13 (3). Male, aged 12 years, was admitted to the hospital on December 16, 1938, with osteomyelitis of the clavicle, duration of symptoms, 3 days. The bone lesion was incised and packed on the day of admission. Patient reacted badly, with prolonged high temperatures. From December 17, 1938, to January 20, 1939, 142 grams of sulfapyridine were given. Blood culture showed *Staphylococcus aureus*  $\alpha$  (70 colonies per c cm). Patient developed a generalized pustular eruption during the postoperative period, with metastases in both humeri and the left tibia. These metastases subsided with wet dressings. During the course of the illness, x-ray films showed progressive destruction in the primary bone focus and the metastases. During this period, in addition to sulfapyridine, 90,000 units of staphylococcus antitoxin were given, as well as a total of 2,750 cubic centimeters of blood. On December 16, 1938, the white blood cells numbered 8,000. During the acute illness the number rose to 23,000, and toward the end fell to 4,000. Patient was finally discharged with all wounds healed. To date, x-ray films have showed progressive regeneration of the bone lesions.

CASE 14. Male, aged 12 years, was admitted to the hospital on June 21, 1938, with osteomyelitis of the ulna, duration of symptoms, 3 days. A subperiosteal abscess over the ulna was incised and packed on June 27, 1938. Wound culture showed *Staphylococcus aureus*  $\alpha$ . Blood culture was negative. The x-ray films taken on admission showed no signs of bone involvement. The wound continued to drain. On July 25, x-ray films showed extensive osteomyelitis of the ulna. On July 27, two thirds of the ulna was resected, the bone was boiled according to the technique of Orell, and reimplanted. On October 14, 1938, part of the reimplanted bone which had formed a sequestrum was removed. The wound continued to drain through sinuses for many months. On March 28, 1940, the wounds were healed. X-ray films showed no union between the remaining bone implant and the residual of the ulnar.

CASE 15. Male, aged 75 years, was admitted to the hospital on October 22, 1938, with osteomyelitis



Fig 3 Case 13. Roentgenograms taken before operation, 2 weeks after, and later showing metastasis to humerus

of the humerus, duration of symptoms, 1 month. The bone was incised and packed on October 22. From October 23 to October 27, 9 grams of sulfanilamide were given, since the wound culture showed *Staphylococcus aureus*  $\alpha$ . Blood culture was negative. The patient developed bronchopneumonia and died on October 28, 1938.

CASE 16. Male, aged 12 years, was admitted to the hospital on March 2, 1938, with osteomyelitis of the femur, duration of symptoms, 6 days. On March 3, a subperiosteal abscess over the lower end of the femur was incised and packed. Wound culture showed *Staphylococcus aureus*  $\alpha$ . From March 2 to March 4, 7 grams of sulfanilamide were given. In spite of that, the temperature remained high. On March 2, hemoglobin was 80 per cent, red blood cells, 5,000,000, and white blood cells, 17,000. On March 4, the number of white blood cells dropped precipitately to 5,150. *Staphylococcus* antitoxin, 27,000 units, as given the next day, as well as a blood transfusion of 900 cubic centimeters. During the postoperative period, the patient developed infectious metastases over the right fibula and in the alveolar process. The alveolar process was relieved



Fig. 2. Case 4. Pre-operative, postoperative, and healed.

*Staphylococcus aureus*. Hemoglobin on September 9 was 94 per cent. white blood cells, 8,500, with normal differential. Symptoms subsided and patient was discharged. Three weeks later there was a similar recurrence which subsided under wet dressings without the use of sulfo drugs. Patient has been symptom-free ever since.

CASE 7. Female, aged 7 years, was admitted to the hospital on March 4, 1939, with osteomyelitis of the humerus of 4 days' duration. Initial ray films showed faint haziness about the proximal metaphysis. On the day of admission, a subperiosteal abscess was packed with vaselin gauze after it was incised. Seventy-two grams of sulfapyridine were given from March 4 to March 7. Blood culture showed *Staphylococcus aureus* on March 5 and as negative on March 5. On March 4, the white blood cell count was 10,000 hemoglobin, 65 per cent. On March 9, the white blood cell count was 8,400 hemoglobin 6 per cent. On March 3, the white blood cell count was 8,600 hemoglobin 50 per cent. On March 8 the hemoglobin was 58 per cent and transfusion of 35 cubic centimeters of blood as given. Serial ray films taken during the stay in the hospital showed progressive destruction of the upper third of the humerus. Patient was readmitted to the hospital on November 7, 1939, with two draining sinuses. On the following day, sequestrum was removed. On April 5, 1940 the patient still presented the draining sinuses. Ray films showed increasing density of the lesion in the bone.

CASE 8. Female aged 3 years, was admitted to the hospital on August 1, 1939, with pain in her chest of 4 days' duration. Ray examination re-

vealed osteomyelitis of ribs. From August 3 to August 5, 1 gram of sulfapyridine was given. On August 20 the bone abscess was incised and packed. Wound culture showed *Staphylococcus aureus* and *Streptococcus hemolyticus*  $\beta$ . Hemoglobin on August 1 was 90 per cent. but blood cells, 7,500. On August 30 hemoglobin was 88 per cent. Blood culture as negative. Ten months later the wound was still draining and the x-ray showed no change in the local lesion.

CASE 9. Male, aged 3 years, was admitted to the hospital on August 14, 1939, with osteomyelitis of the sternum of 4 days' duration. Ten days before admission 4 grams of sulfapyridine were given from August 4 to August 5. On August 7 the lesion at the sternum was incised and drained. Blood culture showed *Staphylococcus aureus* and *Streptococcus hemolyticus*  $\beta$ . On August 4, the hemoglobin was 95 per cent. red blood cells numbered 5,500,000 white blood cells 30,000 sedimentation rate 36 hours. On August 6 the white blood cells numbered 8,000. On December 14, 1939, the wound was entirely healed.

CASE 10. Male, aged 8 years, was admitted to the hospital on July 7, 1939, with osteomyelitis of the fibula of 4 days' duration. This was a recurrence of a lesion eleven years previously and asymptomatic since that time. On July 18, diaphysectomy was performed. From July 9 to July 16, 6 grams of sulfanilamide were given. Hemoglobin as maintained between 55 and 65 per cent during the hospital stay. On August 18, a 500 cubic centimeter blood transfusion was given. Wound culture showed *Staphylococcus aureus*. Following the operation, the wound drained. The temperature persisted at 100 degree level for over month.

CASE 11. Male, aged 33 years, was admitted to the hospital on March 27, 1939, with pain about the hip of 4 days' duration. A diagnosis of osteomyelitis involving the lesser and greater end of the femur was confirmed by the ray. On March 30, the bone lesion was incised and packed. From March 27 to April 1, 10 grams of sulfanilamide were given. The bone incision was further extended on April 7 because of persistent drainage. Blood culture as negative and wound culture showed *Staphylococcus aureus*. On admission, the patient was acutely ill with temperature of 104 degrees F. This fell after the first operation but rose to 103.6 degrees F. week later and continued to rise and fall till the second operation was performed. On March 7 hemoglobin was 7 per cent. white blood cells, 9,700. On April 1 hemoglobin was 64 per cent. white blood cells, 9,700. The wound as still draining at the time of discharge and there was no sign months later of any bone regeneration.

CASE 12. Male, aged 12 years, was admitted to the hospital on March 8, 1939, with osteomyelitis of the upper end of the humerus. Duration of symptoms was 3 days. On the day of admission, the bone was incised and the wound was packed. Blood cul-

# EXPERIMENTAL COLLATERAL CIRCULATION OF THE HEART

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**A**LERT surgeons in their endeavor to relieve Pick's disease by removing constricting pericardial adhesions encountered blood vessels of considerable size traversing between the myocardium and the adhesions (1) This observation led to the belief that possibly a new blood supply to the heart could be produced by surgically grafting various tissues to the heart Consequently, skeletal muscle, omentum, fat, mediastinal tissue, lung, etc were implanted on the heart and, in some instances, vascular connections were demonstrated (2) The most recent of these works is that of H B Burchell who concludes "The possibility that small vascular connections between a graft and the heart might develop to a functioning degree cannot be denied, but in experiments seemingly favorable to such a result it has not occurred"

The natural processes of life bring about the narrowing of the lumina of the coronary vessels and too frequently early dire results are not readily produced in experimental animals Acute and chronic mechanical constrictions of these arteries have been made in the laboratory and the ensuing infarct, degeneration, and thinning of the myocardium and papillary muscles have been observed To offset this pathological process various grafts were implanted on the experimental heart with the hope that new blood vessels large enough to carry sufficient blood would develop to nourish the ischemic areas One must with reservation compare this condition produced in animals having young healthy hearts, adequately nourished and possessing the physiological means of repair and construction, to the human suffering from coronary sclerosis who has none of these in such abundance Nevertheless on the basis of careful experimental work of this nature, surgeons have attempted and with some measure of success treated these diseased hearts I refer

particularly to Beck (3) in this country and O'Shaughnessy of London, England The former prefers to use the pectoralis major muscle and the latter the omentum as the tissue of choice for grafting

The writer in a series of experiments has taken the omentum, intercostal muscles, lung, and internal mammary artery as grafts and after an interval of 3 to 6 weeks, partially interrupted the flow of blood through the main branches of both coronary arteries Electrocardiograms revealed recent infarcts and then, as time went on, a gradual improvement appeared until the tracings approached those of a normal animal The question which arises resolves itself into two distinct problems Has the graft contributed to the healing process by delivering blood to the heart or have the normally present anastomoses enlarged and carried the necessary nourishment? It is a known fact that a considerable communication between right and left coronary arteries exists especially at the apex and that numerous anastomoses are present at the bases of the great vessels between pericardial and coronary vessels

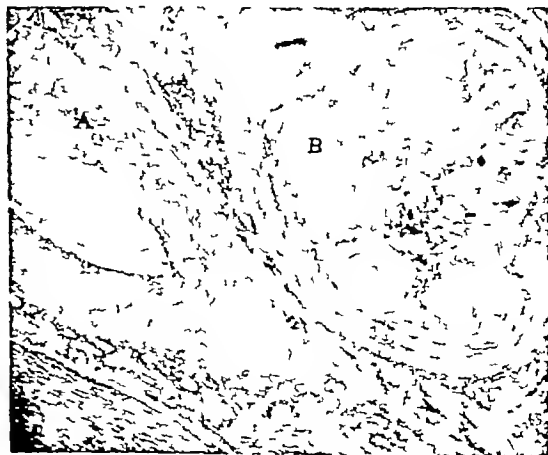


Fig 1 A, coronary artery, B, internal mammary artery

by dental surgery and the fibular process subided with wet dressings.

Cas 7. Male, aged 35 years, was admitted to the hospital on September 3, 1938, with osteomyelitis of the upper end of the humerus, duration of symptoms 5 days. On September 4, bone section was removed, the site of lesion and the wound was packed. Seventy-five cubic centimeters of sulfanilamide were given intravenously in repeated doses on September 3 and 4. The hemoglobin remained about 85 per cent from September 3 to September 5, with two intervening examinations. A blood transfusion of 500 cubic centimeters was given during the postoperative period. Blood culture on September 3 showed *Staphylococcus aureus*, and on September 6 was sterile. During the postoperative period, in spite of immobilization, bone involvement as shown by x-ray studies extended throughout the upper third of the humerus. The wound subsequently healed and later x-ray films have shown increasing regeneration within the lesion.

Cas 18. Female, aged 4 years, was admitted to the hospital on January 4, 1938, with osteomyelitis of the lower end of the tibia, duration of symptoms 3 days. X-ray films were negative concerning any bone involvement at this time. A subperiosteal incision was incised and packed on January 4. On January 5, 4.5 grams of sulfanilamide were given. Hemoglobin varied from 65 to 70 per cent during the hospital stay. A blood transfusion of 500 cubic centimeters was given. Blood culture was negative, and the wound culture showed *Staphylococcus aureus*. During the postoperative period, serial x-ray films showed progressive bone involvement. The wound healed and subsequent x-ray examination showed gradual regeneration of the bone.

Cas 9. Male, aged 15½ years, was admitted to the hospital on July 3, 1937, with osteomyelitis of the femur, duration of symptoms 4 days. In this case 5 grams of sulfanilamide are given between July 8 and July 15. Blood culture was negative. The temperature remained elevated to 103 degrees F. during the early period of sulfone therapy. On July 3, the bone was incised and packed after which the temperature dropped to almost normal within 3 days. Wound culture showed *Staphylococcus albus*. On July 7, the hemoglobin was 50 per cent and the white blood cells 9,000. On July 13, the hemoglobin was 78 per cent and the white blood cells 7,000, showing toxic granules. On July 6, the hemoglobin was 76 per cent and the white blood cells 4,800. X-ray films showed postoperative extension of the area of bone involvement. The wound subsequently healed and has remained quiescent. Later x-ray examination showed progressive bone regeneration.

Cas 20. Female, aged 3½ years, was admitted to the hospital on May 1940, with osteomyelitis of the posterior region of the tibia, duration of symptoms

10 days. On May 1, operation was performed. From May 3 to May 7, 4.5 grams of sulfanilamide are given. Blood concentration of sulfanilamide on May 14 was 4 milligram per 100 cubic centimeters. A plaster boot was applied. Blood culture on May 11 showed *Streptococcus hemolyticus* and sterile on May 4, and again sterile on July 6. Serial x-ray films showed cycle of bone regeneration. Patient has had no recurrence since that time.

## CONCLUSION

On the basis of 20 cases of hematogenous osteomyelitis, and until the above observations are invalidated by a larger series, the following conclusions are presented.

1. The addition of sulfanilamide or sulfapyridine to the treatment of hematogenous osteomyelitis has not significantly altered the general course of bone pathology, rate of recurrences, or metastases.

2. In a series of 20 cases representing all degrees of severity, there was only 1 death and that due directly to sulfapyridine. In several instances toxicity was favorably influenced and the use of the drug was probably the determining factor between life and death.

3. In the treatment of hematogenous osteomyelitis sulfone chemotherapy is not a substitute for surgical judgment, operative technique, or meticulous after-care.

## BIBLIOGRAPHY

- BAWEN, H. P. Acute hematogenous osteomyelitis of the long bones. *Ann. Surg.* 1939, 99, 596.
- KAY, J. A. Rational treatment of acute hematogenous osteomyelitis. *J. Am. M. Ass.* 1938, 113, 63.
- LEWIS, W. D. Fulminating staphylococcus aureus sepsis treated with staphylococcus antitoxin and sulfapyridine. *J. M. Soc. Hosp.* 1940, 6, 318.
- LEWIS, E. Ueber Osteomyelitis Experimentelle. *Zentralbl. f. Chir.* 1895, 37.
- MITCHELL, A. Treatment of acute osteomyelitis by ultron. *Brit. M. J.* 1938, 100.
- PIEDRAITA, D. B. The modern treatment of pyogenic osteomyelitis. *Bull. N. Y. Acad. Med.* 1940, 16, 20.
- ROSENTHAL, N., and VOGEL, P. Genotoxicity produced by sulfapyridine in children. *J. Am. M. Ass.* 1939, 113, 534.
- WIEDELAUF, M. Zur Behandlung der akuten hämatogenen Knocheninfektionen und der Osteomyelitis mit Protosol. *Deutsche med. Wchnschr.* 1938, 64, 854.
- WILKINSON, A. O. *Osteomyelitis*. New York: The Macmillan Co., 1934.
- Idem. Acute hematogenous osteomyelitis: classification of cases as determined by therapeutic indications. *Arch. Surg.* 1937, 11, 320.



Fig 4 This plate represents a case in which the pericardium was not removed. As the opaque mass was being injected it could be seen to pass along the intercostal arteries of both sides thence to the graft, pericardium, and some into the circumflex branch, *A*, of the left coronary artery

lateral. The former received its nourishment through the internal mammary artery and the latter through the intercostal artery. Having prepared the graft, the pericardium was opened, the epicardium and parietal pericardium roughened with a rasp, and the graft sutured with plain No. 00 catgut to the heart. The pericardial sack was left open. The chest wall was then closed over artificially inflated lungs.

The animal was again operated upon at 4 and 8 week intervals when branches of the right and left coronary arteries, respectively, were partially obliterated by silver clips.

Approximately 4 weeks after this interference with coronary circulation, the animal was sacrificed and the specimen was injected with a radio-opaque substance. We endeavored to isolate the heart in such a manner that



Fig 5 The photomicrograph shows the fibrosis between the graft and the myocardium. *A*, skeletal muscle, *B*, area fibrosis, *C*, myocardium.

the injection mass could not enter the coronary circulation except by way of the graft (Figs 3 and 4).

Bismuth oxychloride and acacia were injected into the cannulas as illustrated in Figure 2.

*Graft of omentum to the heart.* To illustrate this type of procedure the protocol of Dog 10 follows. The anesthesia used was the same as on previous experiments. The omentum was brought into the chest cavity through an opening in the left side of the diaphragm and sutured to the heart as were the muscle grafts. This operation was performed on September 20, 1939. On September 27, 1939, a silver clip was placed on the descending ramus of the left coronary artery. At frequent intervals electrocardiograms were made, as illustrated in Figure 6.

September 25, 1939. Normal sinus rhythm, rate 125. Prominent *Q* wave in all leads and in leads II and III the *S*-wave are even more prominent. *S* *T*<sub>1</sub> and *S*-*T*<sub>2</sub> are practically iso electric. *S*-*T*<sub>2</sub> tends to slope downward, *T*<sub>1</sub> is flat, *T*<sub>2</sub> and *T*<sub>3</sub> are diphasic, *P*-*R*, 0.11, *QRS*, 0.07.

October 16, 1939. Ventricular tachycardia frequently interrupted by auricular and *A*-*V* nodal beats. The rate varies constantly but averages 220. In leads II and III the *QRS* complexes are slightly widened, somewhat bizarre in shape and notched at the peak. There is no demonstrable *S*-*T* segment as the downstroke of the sharply inverted *T*-wave is practically a continuation of the descending limb of the *R* complex. *QRS* equals 0.10.

October 27, 1939. Leads I and II only. Marked sinus arrhythmia, rate 65. *P*<sub>1</sub> iso-electric. *P*<sub>2</sub> con-

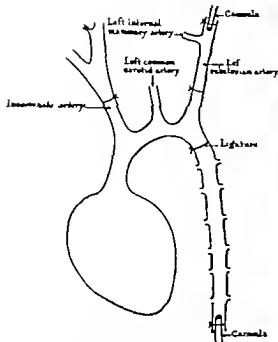


Fig. 1. Injection of barium erythrochrome and suture.

Several special conditions were noted in the postmortem examination of the dogs used in these studies. When muscle was grafted to the heart the graft became quite stiff and the heart action was not free although this apparently did not inconvenience the animal. Omental grafts remained soft and pliable leaving the heart to act more normally.

Microscopic studies of blocks of tissue removed showed some degeneration of skeletal muscle and in all cases an avascular fibrous layer between graft and myocardium (Fig. 5).

Opaque masses entered the coronary tree on several occasions only when the pericardium was not removed. The material reached the coronary arteries through the normally present but enlarged anastomoses between the pericardio-phrenic branches of the internal mammary artery and the coronary arteries and through small anterior branches of the thoracic aorta which gave off branches to the lateral and posterior surface of the parietal pericardium. These small anterior branches also anastomose freely with bronchial phrenic intercostal and internal mammary arteries.



Fig. 3. This plate represents case 1a. Note the pericardium as removed. The graft is fairly vascular but some of the opaque material entered the coronary vessels. 1. Interostial muscle graft. B. heart.

*Anastomosis of left internal mammary artery to coronary artery.* Our first experiments were two attempts to anastomose directly the left internal mammary artery to the descending ramus of the left coronary artery. Both of these procedures failed. The photomicrograph (Fig. 1) shows the close proximity of the two vessels but there is no communication between them. The walls are practically touching each other with only a small strip of exudate between. The coronary artery 4 is patent. The internal mammary artery B contains a recent thrombus. With the use of heparin and an improved technique this type of anastomosis might be possible.

*Suture of intercostal muscle and vessels to the anterior surface of the heart.* The anesthesia consisted of intratracheal ether oxygen mixture and artificial respiration. In these experiments two types of grafts were used one with a pedicle medial and the other with the pedicle

sharply inverted  $T_2$  remains upright and notched at the peak  $T_2$  increased in amplitude and sharply peaked  $P-R$ , 0.10,  $QRS$ , 0.06 Characteristic of recent infarct

December 15, 1939 Sinus arrhythmia, rate 95  $Q$  waves again present in all leads  $S_2$  and  $S_1$  less prominent than on previous tracings  $S-T_1$  and  $S-T_2$  slightly depressed and convex downward  $S-T_2$  slightly depressed  $T_1$  has turned upright but is of small amplitude  $T_2$  and  $T_3$  have turned upright  $P-R$ , 0.11,  $QRS$ , 0.06 Indicated marked improvement in coronary circulation Residuals of previous infarction practically disappeared

On December 18, 1939, the animal was anesthetized and bled to exsanguination through the left carotid artery This specimen was examined carefully both before and after it was injected and cleared first India ink and then red cinnabar (in water) were injected into the central stump of the left common carotid artery after the innominate artery, the left subclavian artery and the common iliac arteries were tied off

There were firm adhesions of the omentum and parts of the pericardium to almost the entire ventral aspect of the ventricular portion of the heart There were many blood vascular anastomotic connections between omental, pericardial, and myocardial vessels These anastomoses were most numerous along the area normally supplied with blood along the branch of the left coronary artery and at the left basal region of the right ventricle The anastomoses were large enough that the ink passed through the lumens of them but no evidence could be found that the cinnabar particles passed entirely through the lumens of any of them to reach the myocardial vessels The clip on the left coronary artery was found near the base of the anterior branch of this artery The clip had almost completely occluded this artery

#### CONCLUSION

Our experiments tend to show

1 The direct anastomosis of internal mammary artery to the coronary might be possible

2 The omental graft lends itself best as a possible source of extracardiac blood supply to the myocardium The graft remains pliable and the heart action is free

3 Muscle grafts become quite firm, interfere with heart action and a layer of fibrosis develops between skeletal and myocardial muscles

4 The heart of the healthy dog withstands diminution of its normal blood supply until it reaches the point of infarction and then recovers as demonstrated by the electrocardiogram

5 Vascular connections between the graft and the heart muscle can be demonstrated in microscopic dissections

Additional experiments are being carried out at the present time further to prove these contentions

The writer wishes to acknowledge the assistance of Dr Chester M Kurtz who interrupted the electrocardiograms, Dr P F Swindle who injected omental graft specimen and Dr Elmer Franseen who gave much time and effort in the early phases of this work

#### REFERENCES

- 1 BECK, C S The development of a new blood supply to the heart by operation *Ann Surg*, 1935, 102 801-813
- 2 Idem Further data on the establishment of a new blood supply to the heart by operation *J Thoracic Surg*, 1935, 5 604, 1937, 6 611
- 3 Idem Coronary sclerosis and angina pectoris, treatment by grafting a new blood supply upon the myocardium *Surg, Gynec & Obst*, 1937, 64 270-272
- 4 BURCHELL, H B Adjustments in coronary circulation after experimental occlusion *Arch Int Med*, 1940, 65 240-262
- 5 O'SHAUGHNESSY, L Surgical treatment of cardiac ischemia *Lancet*, 1937, 1 185-194



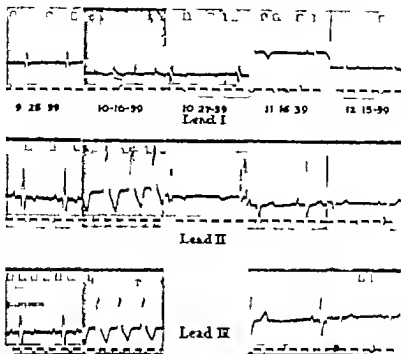


Fig 6 Electrocardiogram in experiment dog  $\alpha$ , osseum graft

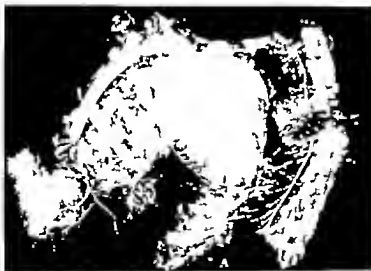


Fig 7 Roentgenogram of an osseum heart graft injected specimen  $\alpha$  osseum

considerably lower than on September 26 1939.  $Q$  relatively more prominent than on previous tracings.  $Q_2$  slightly less prominent and  $S_2$  is definitely less prominent.  $ST$  depressed and tends to slope downward.  $S-T$  depressed.  $T$  is low and diphasic.

$T$  is diphasic but chiefly inverted (similar to September 26 1939).  $PR$ ,  $QRS$  06.

November 6, 1939. Marked sinus arrhythmia, rate 95.  $Q_1$  has disappeared. Small  $Q_2$  and  $Q_3$  present.  $ST$  very slightly elevated.  $T$  has become

sharply inverted  $T_1$  remains upright and notched at the peak  $T_2$  increased in amplitude and sharply peaked  $P-R$ , 0.10,  $QRS$ , 0.06 Characteristic of recent infarct

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- 4 BURCHFIELD, H B Adjustments in coronary circulation after experimental occlusion *Arch Int Med*, 1940 65 240-262
- 5 O'SHAUGHNESSY, L Surgical treatment of cardiac ischemia *Lancet*, 1937, 1 185-194

# PERICARDIECTOMY FOR CHRONIC CONSTRICTIVE PERICARDITIS

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THE fibrous tissue deposited in constrictive pericarditis results from a previous infection and produces symptoms as the constriction of the heart increases. The deposition of constrictive tissue may involve the pericardium or epicardium, but usually involves both in such a way that the two layers are adherent. Analysis of a large number of cases, reported in the literature reveals the fact that about 20 per cent of them can be proved to be tuberculous in origin the others are secondary to an infective process, of which the respiratory group, e.g. influenza, is important. It is agreed by most authorities making a study of the disease that rheumatic fever is not a primary factor. The disease has been popularized on the continent by Volhard and Schmieden and in this country by Churchill White Beck, and others. The disease is readily confused with diseases such as congestive heart failure hepatic cirrhosis etc. even by trained cardiologists, as is suggested by the fact that it is being recognized and treated in a relatively small number of clinics. It is the chief purpose of this paper to attempt to point out the manifestations and laboratory procedures which will lead to a minimal amount of error in diagnosis.

## CLINICAL MANIFESTATIONS

Perhaps the earliest symptoms complained of are weakness and dyspnea. The dyspnea, however is usually noted only upon exertion not being significant while the patient is resting or lying down. As soon as these symptoms develop ascites and edema of the extremities are noted. Usually the ascites precedes the edema of the extremities by several weeks or months. Loss of weight generally occurs, but may not be appreciated by actual weight fig-

ures because of the development of ascites. Tachycardia particularly upon exertion is fairly constant. Fever is absent. There may be a complaint of mild epigastric distress with anorexia. In the advanced stages of the disease slight anemia and a decrease in blood proteins, with a tendency toward reversal, will be noted.

Upon examination one of the most significant findings will be dilatation of the jugular veins, with or without pulsation. Heart sounds are faint but rarely are murmurs present. A paradoxical pulse (thrummy in volume during inspiration) is fairly consistent. The blood pressure is low and the pulse pressure diminished. In addition to ascites, fluid is usually encountered in the pleural cavity. It was this feature of the disease which Pick stressed when he originally reported observations on the syndrome. Rarely will Broadbent's sign be encountered unless adhesive pericarditis is also present. Aural fibrillation is occasionally encountered. Electrocardiograms usually reveal low voltage inversion or flattening of the T waves in leads one or two or both. In 2 or 3 patients, upon whom blood volume findings were made by Burwell and Blalock the volume was found to be 30 to 45 per cent above normal. Cardiac output, however is lower than average. Circulation time is delayed varying between 30 and 60 seconds—normal, 15 to 20. Venous pressure is consistently high ranging between 13 and 35 centimeters of water—normal is 5 to 10. The liver is enlarged particularly in the advanced cases, and as Harrington and Barnes have noted liver function tests will show definite impairment of function. Upon examination the heart shows no enlargement, and in fact frequently is smaller than normal. There may be slight distortion of the lines of the cardiac shadow. In so far as some of the normal curves are straightened (Fig. 2a) About 20

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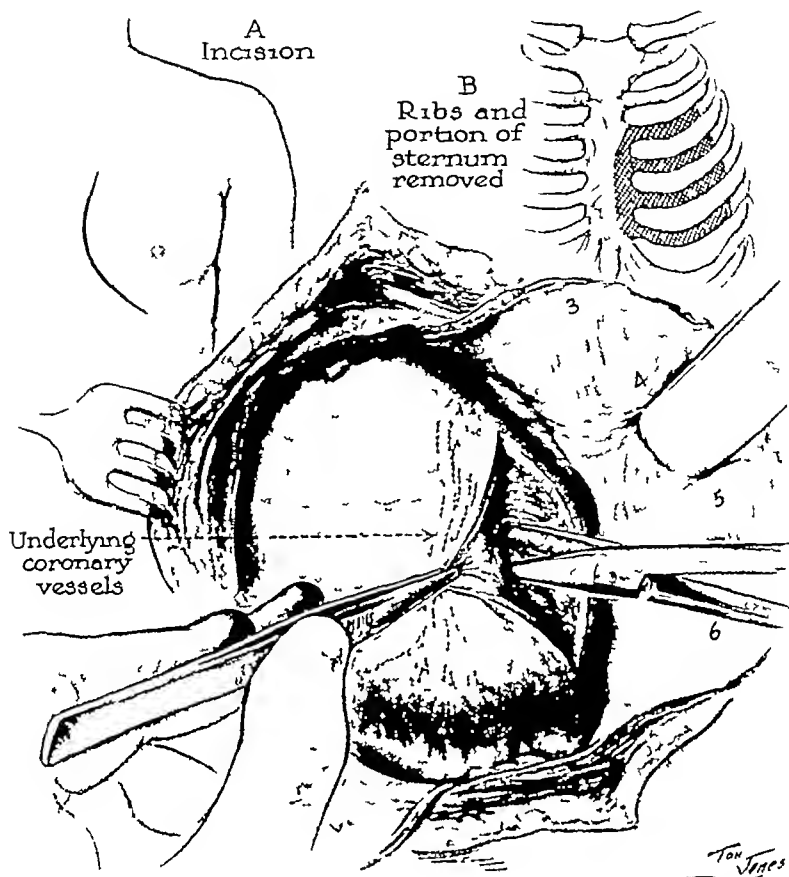


Fig 1 Excision of the scar should be started over the left ventricle, and an attempt made to find a plane between the scar and cardiac muscle. All landmarks are usually obliterated, but the coronary vessels are illustrated by dotted lines to reveal their relative location. Injury to the coronary artery is dangerous but may be difficult to avoid, for occasionally it is buried in the scar. Insert A shows the type of incision, B, the area exposed and amount of sternum removed in the cases herein reported.

per cent of the patients with constrictive pericarditis have calcified plaques in the thickened pericardium and will be manifested in the x-ray film. Fluoroscopic examination usually reveals decrease in pulsation, particularly on the right side. This lack of pulsation will be best demonstrated by kymographic roentgenogram (Fig 3a).

#### DIAGNOSIS

Perhaps the disease most readily confused with constrictive pericarditis is congestive heart failure. Valvular diseases will rarely be difficult to eliminate because of the presence of murmurs, which are absent in constrictive

pericarditis. Although dyspnea is common in congestive heart disease, it is not diminished upon rest and lying down as markedly as it is in constrictive pericarditis. Of more importance also is the fact that ascites develops early in constrictive pericarditis, usually preceding the edema of the extremities, in contrast to its significance in congestive heart failure. Fluid is frequently found in the pleural cavities. The liver is usually enlarged. Of still greater importance in differentiation is the normal or slightly decreased shadow of the heart. With equal symptoms, the cardiac shadow in congestive heart failure will be enormously enlarged, whereas it is of normal



Fig. 2a. Roentgenogram of chest of patient in Case 1, before operation. Not the small heart and straight left border high as palpating very little on fluoroscopy.



Fig. 2b. An x-ray picture taken 1 month after operation suggests that the heart has shifted upward but may still be fixed at point on the left border.



Fig. 2c. An x-ray picture taken 3 months after operation reveals normal shape with obliteration of the straight, fixed left border.

size or slightly smaller in constrictive pericarditis. Although distention of the jugular veins, elevation of the venous pressure and delay in circulation time may be encountered in congestive heart failure they are of diagnostic importance in constrictive pericarditis because of their frequency. The almost universal presence of a paradoxical pulse in constrictive pericarditis will be helpful in making the diagnosis. When calcification is present

in the pericardium the x-ray examination alone will make the diagnosis.

#### OPERATIVE CONSIDERATIONS

In 1902 Brauer suggested removal of the ribs and costal cartilages from the area over the heart. This operation was performed for constrictive pericarditis, and although a high incidence in improvement in symptoms was noted in a survey by Smith and Liggett, the operation is definitely inferior to actual removal of the constricting fibrous tissue. We are indebted to Delorme and Rehn for the development of the modern operation with removal of the constricting fibrous tissue.

Incision should be started slightly to the left of the sternum at the level of the second rib and curved toward the sternum and out laterally as the level of the sixth and seventh ribs is approached. Although local anesthesia may be used it is the opinion of most men including the present authors, making a study of the disease that a general anesthetic is preferable. The fourth, fifth and sixth costal cartilages and ribs are resected subperichondrially and subperiosteally. The intercostal muscles are cut away from the sternum care being used not to devitalize any of the tissue because it is of great importance in filling up dead space when the wound is closed. The

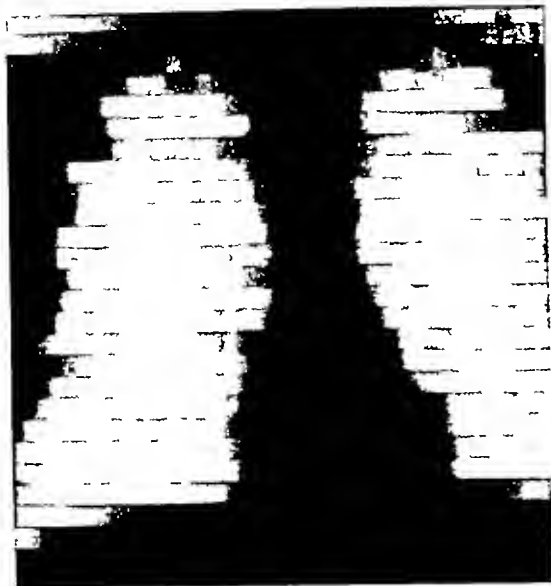


Fig 3a Roentgen kymogram of Case 1, before operation. Note that pulsation is diminished on both borders of the cardiac shadow.



Fig 3b A roentgen kymogram 3 months after operation reveals fairly pronounced and seemingly normal pulsation on each cardiac border.

internal mammary artery and vein should be ligated proximally and distally. Although some surgeons (Heuer) do not believe partial resection of the sternum is necessary, most, including the present authors, are in favor of removing the left half to facilitate exposure, particularly in excising the scar over the lateral surface of the right ventricle. The reflection of the left pleura is located and dissected outward along with adjacent tissue to allow exposure of the heart. As soon as the heart is exposed, attempt should be made to identify the descending branch of the left coronary artery and the auriculoventricular groove. Usually, however, all landmarks will be obliterated. Worse than this, as Burwell and Blalock have demonstrated, the descending coronary artery itself, is frequently imbedded in the scar, as it was in one of our cases, and may be injured during excision of the scar. Churchill is of the opinion that the scar should be carefully removed from the region of the auriculoventricular groove, but the authors wish to caution that this procedure must be done with extreme care because of the thinness of the auricular wall at the junction. Most authors, and we agree, do not believe

it is necessary to remove the scar from the auricles, or the great vessels, unless the scar is markedly more pronounced here than elsewhere. The essential features consist of removal of the scar from the ventricles and from the apex. The apex is usually densely adherent to the diaphragmatic surface, and it is exceedingly important that this be freed. The excision of the scar over the ventricles should be started on the left side because of the danger of dilatation of the right ventricle if excision is started on the right side. Areas of calcification should be removed only if this can be done safely. Occasionally, the calcified plaque will extend deep into the ventricular wall. Removal might leave such a thin layer of muscle that perforation would develop.

Manipulation of the heart tends to produce arrhythmia. It is exceedingly important, therefore, that if the rhythm of the heart becomes disturbed, all operative manipulation should be terminated until normal rhythm is regained, restitution to a normal rhythm rarely requires more than a minute or two. During the process of excision of the scar a flap of fibrous tissue should be left attached to the heart so that it might be inserted firmly

against any bleeding point whether it be perforation of the ventricle or incision through the descending branch of the left coronary artery. The importance of this precaution was appreciated in Case 1 reported herein when a sudden, severe hemorrhage developed during excision of the scar over the left ventricle. Removal of the scar should be as complete as possible but should not be extended laterally beyond the limits of good exposure because of danger of hemorrhage which could not be controlled with inadequate exposure. If the pleural cavity on either side is entered, the hole should be obliterated immediately and a suture taken to close it. Rarely will this jeopardize the patient's condition to any significant degree.

The dead space created by excision of the ribs is sealed up as well as possible with the pectoral and intercostal muscles. A small rubber drain should always be left in the inferior or superior part of the wound to prevent accumulation of fluid.

One of the most important considerations in postoperative care is oxygen therapy which may be administered by a tent, mask, or nasal tube. Elevation of the back rest of the bed will add to the comfort of the patient. Intravenous fluids should be given with caution because of the severe, sudden strain thrown on the heart incident to the operative procedure. The authors are of the opinion however that a small transfusion in addition to 500 to 700 cubic centimeters of glucose given

slowly is safe and even advisable. Fluids and food are administered as tolerated. Digitalis may be used in the presence of fibrillation but we do not favor its administration for tachycardia alone.

**CASE.** H. P. No. 62,792, 41st laborer, 35 years of age, was admitted to the Illinois Research and Educational Hospital, August 29, 1938, complaining of abdominal swelling and edema upon exertion. Eighteen months before admission he had an acute ailment with fever, generalized chills, pharyngitis, and albuminuria followed in a few weeks by epigastric distress and generalized edema. Progressive weakness was major complaint. Abdominal paracentesis as performed several times during the last few months before admission to this hospital. At the time of admission to this hospital, abdominal distention—ascites—was sufficient to cause discomfort, but there was no orthopnea.

The temperature as normal, the pulse small and 85 to 95 per min. The blood pressure as 6 systolic and 00 diastolic. No cervical veins visible. The lungs are resonant and free from rales. The pericardial impulse as within the mid-clavicular line and there was slight retraction to the left during systole. The rhythm as regular. The liver was firm and not tender. It extended about 5 centimeters below the costal margin. The spleen was not palpable. The routine urinalysis, blood counts, and serology showed normal findings. The serum proteins were albumin 3.0 globulin 3.45 grams per cent. Fluoroscopic examination demonstrated restricted motion of the heart except at the pericardium. The meter chest film showed small heart, the right and left borders being straight, thus giving a "U" edge shape. A roentgen-lymvanogram confirmed the fluoroscopic findings. The venous pressure as 15 centimeters, the decubital circulation time 35 seconds, and the ether time 6 seconds. Abdominal paracentesis yielded 6.5 liters of straw-colored fluid which contained 4.37 grams per cent of total protein. Bacteriological examination—including guinea pig inoculation—was negative. The Mantoux test and 5 cubic centimeter of old tuberculin 00,000 gave a strongly positive reaction. The central necrosis. The electrocardiogram showed low QRS, the first lead and inverted T waves in the three standard leads. The T<sub>1</sub> was low. A diagnosis of constrictive pericarditis was made.

Pericardial resection was performed October 3, 1938. The pericardium was adherent everywhere to the heart, but adhesions over the antricles were filmy and readily broken. No landmarks were visible because of the dense scar. The pericardium as attached to the diaphragm. In dissecting through this scar was opened into a cystic cavity containing about an ounce of brownish fluid (thick fibrous material). The pericardium as so adherent to the heart muscle that it could be removed only by sharp

TABLE I.—VENOUS PRESSURE, CIRCULATING TIME AND VITAL CAPACITY CASE

|                | Venous pressure cm. | Circulating time (phlebogram) sec. | Vital capacity cm. |
|----------------|---------------------|------------------------------------|--------------------|
| August, 1938   | 75                  |                                    | 2600               |
| September 1938 | 75                  |                                    |                    |
| October, 1938  | 55                  | 58                                 |                    |
| November, 1938 | 80                  | 57                                 | 2000               |
| December 1938  | 23                  |                                    |                    |
| January 1939   | 16                  | 50                                 |                    |
| July 1939      | 16                  | 55                                 |                    |
| September 1939 | 15                  | 51                                 | 5500               |
| January 1940   | 1                   | 50                                 |                    |

The pericardial resection as performed Oct. 25, 1938.



Fig 4a Roentgenogram of chest of the patient in Case 2. Note that the heart shadow is of a relatively normal size.

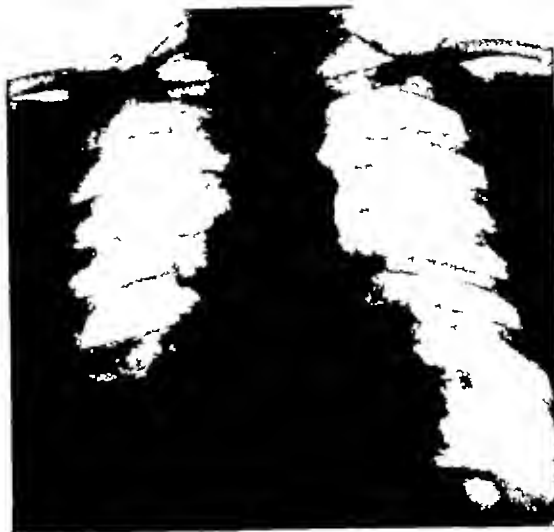


Fig 4b Case 3, no operation, few small cavities containing turbid fluid yielding tubercle bacilli on smear found within pericardial sac at autopsy.

dissection. During the process of cleaning the left ventricle a severe hemorrhage was encountered. A flap of fibrous tissue was rapidly inserted against this point, and two sutures were applied. This controlled the hemorrhage. We removed the scar as far laterally on each side as was deemed safe and freed the apex from the diaphragm. The wound was then closed, interrupted catgut was used and a drain was inserted at one point. The postoperative course was without complications except for a moderate rise in temperature— $101$  to  $103^{\circ}\text{F}$ —and the development of a left pleural effusion. Thoracentesis 7 days after operation yielded 1200 cubic centimeters of fluid which contained a few polymorphonuclears, but no organisms were recovered. Later a thoracentesis was repeated. Abdominal paracentesis was never necessary after the operation. Roentgen-kymogram taken 2 months after the operation showed good movement of the ventricular borders. Chest films taken at intervals during the year following operation demonstrated a gradual development of a normal curvature of the ventricular borders and an increase in the heart size toward normal. Symptomatic improvement continued for at least a year after operation. This was demonstrated both in increased exercise tolerance and in a gradual drop in the venous pressure. Table I gives the values for venous pressure, circulation time, and vital capacity. An electrocardiogram taken  $1\frac{1}{2}$  years after operation showed better amplitude, but T<sub>2</sub> and T<sub>3</sub> still were deeply inverted. When last seen 2 years after operation he was working full time, and claimed that normal strength and physical reserve had returned.

CASE 2. E. G., No 70,765, of Dutch descent, age 53 years, was admitted to Illinois Research Hospital, on February 29, 1940. His symptoms

were first noted in September, 1936, at which time he complained of dyspnea on exertion. Soon he was unable to walk more than a block without marked fatigue and dyspnea, this was followed by edema of the ankles, but ascites did not develop until 2 months later. With bed rest the ankle edema subsided, but the ascites did not, he remained an invalid henceforth, being unable to be out of bed except for short intervals. Abdominal paracentesis was performed on several occasions by outside physicians before entry to the Illinois Research Hospital. His past history was not significant. He had not had rheumatic fever, nor any known tuberculous lesion.

On examination it was noted that there was no fever, the pulse was 90 and its volume became small with inspiration—paradoxical pulse. There was no dyspnea at bed rest but slight exertion caused marked dyspnea. There were cyanosis and a slight icteric tint. The abdomen was protuberant. The blood pressure was 104 systolic, 72 diastolic, when supine, standing it was 104 systolic and 84 diastolic. There were very prominent, distended, pulsating cervical veins. The veins over the lateral thorax and arms were also distended and prominent. Except for flaring of the costal margins and elevation of the diaphragm the lungs were normal. Cardiac dullness was found 20 centimeters to the right of the parasternal line and to the midclavicular line on the left. The apex beat could not be made out. The tones were normal but slightly decreased in intensity, there were no murmurs. Ascites was present, the liver was palpable three finger breadths below the costal margin, and it was firm and not tender. The spleen was not palpable. Moderate ankle edema was present. There was no clubbing of the nails.



The urine was normal, the blood contained 15 grams per cent hemoglobin, red blood cells, 4,400,000; hit blood cells 700. Wassermann and Kahn tests gave negative reactions. The serum albumin was 3.67, the globuli 4.69, the icterus index. The venous pressure at the antecubital vein was more than 30 centimeters. The decubiti circulating time was 20 seconds and the ether time 3 seconds. The vital capacity was 600 cubic centimeters. After removal of .8 liter of ascitic fluid the vital capacity was 2600 cubic centimeters. The tuberculin test—0.1 c.cm. of old tuberculin, 0.0001—gave an area of redness and slight induration 4 centimeters across. The electrocardiogram showed the QRS waves to be low and slurred and the T waves low and diphasic in the standard leads. The QRS 4 as slurred, T4 low and diphasic. The meter chest film showed normal heart size, a straight right heart border, an unusual configuration of the left, and evidences of pleural fibrosis. Fluoroscopy showed limited movement. Roentgen-lymography showed decreased but absent movement of the right ventricle, good movement in the upper portion of the left ventricle, but restricted movement in the apex.

Pericardial resection was done on March 7, 1930. Exposure of the heart revealed all landmarks gone. The auricles were enormously distended. The ventricles were squeezed down to mass not much larger than lesion by the dense scar tissue. The excision of the thickened pericardium was started over an area which appeared to be the left ventricle. Further dissection of scar tissue was carried to the lateral border on each side. The cardiac muscle was so cyanotic and appeared so friable that we were much discouraged as to the outcome. Neither did the heart bulge out through the opening in the scar tissue as much as we expected. The wound was closed with silk, without drainage. Accumulation of fluid the following day made it necessary for us to insert drain between some sutures.

Patient was sent to the ward and given oxygen therapy. Condition remained unchanged for several days, but 14 weeks after operation, he developed increased signs of cardiac decompensation and died 4 days later with exacerbation of his symptoms.

CASE 3. B. W. N. 68 years, male, aged 64 years, was admitted to the Illinois Research and Educational Hospital, September 7, 1930. He had been comparatively well until May, 1929, when he noticed fatigue and weakness, associated with cough, which was occasionally productive of tenacious yellow sputum. Anorexia became marked and he rapidly lost 45 pounds in weight. In June he developed dyspnea, ascites, and edema of the legs. With increasing ascites he developed pain in the upper abdomen. The blood pressure was 140 systolic and 90 diastolic, the pulse 90, and the temperature normal. There was pleural effusion on the right and crepitant rales at the left base posteriorly. The heart borders were found thin normal limits. There were no murmurs. Moderate ascites was present. A mass believed to be the liver extended to

the umbilicus, it was firm and tender. Pitting edema was present at the ankles. Roentgen examination of the chest after thoracentesis showed evidences of pulmonary congestion and some fluid in the right pleural space. The transverse thoracic diameter was 30.6 centimeters and the largest transverse cardiac diameter was 13.3 centimeters. The specific gravity of the pleural fluid was 1.02, the protein content .46 grams per cent. Smears were negative. The culture of the pleural fluid was negative, guinea pig inoculation was negative. The tuberculin test using 0.1 c.cm. of 1,000 old tuberculin intracutaneously was positive. The venous pressure taken on October 2, 1930, gave a value of 30 centimeters. Decubiti circulating time was 24 seconds, the ether time 25.4 seconds. Urinalysis showed trace of albumin and occasional pus cell. The hemoglobin was 16.5 grams per cent, the red blood cells, 5,300,000, white blood cells, 6,750. The Wassermann and Kahn test were negative. The serum albumin was 3.6 per cent and the globulin 8 per cent. The icterus index normal. The electrocardiogram showed low QRS complexes and low diphasic T waves in the standard leads.

Because of the patient's age, the pulmonary congestion, and failure of fluoroscopic examination to reveal restriction of cardiac movements, diagnosis of cardiac decompensation due to myocardial insufficiency secondary to arteriosclerosis was accepted in preference to constrictive pericarditis.

Decompensation progressed. Repeated thoracenteses and abdominal paracenteses were necessary in the course of the disease. Painful mass developed in the right lower quadrant. Death occurred on February 1, 1930.

A autopsy showed firm cartilaginous pericardium reaching thickness of millimeters and inseparably fused to the epicardium. The scarred pericardium contained several small collections of milky fluid. Smears of this fluid showed numerous acid fast organisms which on culture were found to be tubercle bacilli. The outer surface of the pericardium was smooth. The coronary arteries were patent throughout but contained an occasional thrombotic deposit. There was also tuberculous peritonitis with the omentum formed into thick mass across the upper abdomen. The mass in the right lower quadrant was composed of several adherent loops of bowel. There was milky tuberculous of the liver, kidney, spleen, adrenals, retroperitoneal nodes, and lungs. From the autopsy findings it was evident that the tuberculous pericarditis was of much longer duration than the tuberculous peritonitis.

#### IMPORTANT POINTS IN DIAGNOSIS AND TREATMENT

Beck has stressed the physiological concept that the heart in constrictive pericarditis is a heart under compression. It is a small one

imprisoned by the constricting adhesions. Its embarrassment is caused by an inability to hold in diastole sufficient blood to maintain an adequate arterial circulation. Hence the cardiac output (Heuer and Stewart) of necessity falls and under exertion the heart rate increases as a compensatory adjustment. When the output falls excessively, there is a discrepancy between the blood volume and the vascular bed. The vasomotor center becomes unable to reduce the arterial bed correspondingly and the blood pressure falls. The circulation is inadequate and it can be readily appreciated that these patients will first complain of indefinite symptoms, as easy fatigability, slight dyspnea after exertion, and later, more and more serious limitation of activity. When they are examined at this stage the heart borders are normal both on physical and fluoroscopic examination. Usually no murmurs are heard, and the circulatory inadequacy is attributed to myocardial weakness with a loss of cardiac reserve. The patient is considered to have a decompensation which produces symptoms but, as yet, no signs.

As the condition progresses and the compression becomes more severe, the blood piles up in the vena cava, and gradually backs into the finer systemic venous radicles. The venous pressure in the vena cava which normally is negative, becomes positive, and continues to rise until it exceeds the limiting pressure exerted on the relaxing auricle. When it is in excess of the intrapericardial pressure the blood flows in to fill the auricles. The height of the venous pressure gives one an index of the severity of the cardiac compression. The antecubital venous pressures in the 3 cases were, respectively, 26, 30, and 30 cubic centimeters of salt solution. With the increasing venous pressure the blood accumulates in the first available reservoir. All the systemic veins have valves and these combined with the pumping effects of muscular action tend to keep the blood flowing towards the heart. The hepatic veins are without valves and the liver is readily distensible so it first receives the extra blood. The liver then becomes congested, large, tender, and establishes a portal decompensation. With long continued con-

gestion liver damage occurs, producing varying pathological pictures, ranging from fatty livers through fibrosis to cirrhosis. It is interesting that the spleen is not usually palpable. When the patient is seen at this stage of the disease he presents a normal sized heart without murmurs, prominent veins, ascites, and a large liver. After paracentesis, the spleen is still not palpable. A plate of the chest shows no evidence of pulmonary congestion. The abdominal findings are so striking that the distention of the veins, unless marked, is overlooked. Even if the patient complains of dyspnea this also is easily attributed to a lowering of the vital capacity by upward pressure from the distended abdomen. Hence the ascites now stands out as the prominent symptom demanding explanation. If the patient is middle aged, the diagnosis of cirrhosis becomes probable. The liver function tests, however, do not indicate as much damage as would be expected in a frank cirrhosis. The spleen also is not palpable. Hence, carcinomatosis with fluid formation and tuberculous peritonitis will be considered. The ascitic fluid will have a lower protein content than would be expected in these conditions and the clinical course will have been too protracted to render the diagnosis of carcinomatosis tenable. A tuberculous peritonitis is eliminated with much more difficulty. In fact, it existed in Case 3 along with a tuberculous pericarditis. At this point the patient is re-examined carefully. The prominent veins are again noted, a venous pressure reading is taken. This is increased and rises still higher when pressure is exerted over the liver. The correct diagnosis is now possible, and should be made.

As the condition progresses there is added to the picture a generalized edema beginning in the feet extending later to the arms, face, and body. This represents a more advanced stage of venous stasis. The blood volume will be increased. The circulation time will be prolonged. Since these findings are present in all cases of congestive heart failure, the significance of an increased venous pressure is lost. The diagnosis still should be made at this stage. Cardiac decompensation does exist. The point at issue is the cause of the decompensation. If the patient had a rheu-

matic valvulitis or arteriosclerotic heart disease with myocardial damage, one would expect to find a heart somewhat larger than normal and a lung which shows passive congestion. This passive congestion would be revealed by transitory attacks of blood tinged expectoration and by an x ray plate revealing pulmonary congestion. In constrictive pericarditis the blood does not get into the heart and the quantity which does get into the aunele is readily pumped into the arterial circulation. There is therefore, no opportunity for blood to accumulate in the lung. On the other hand a clear lung is not compatible with a diagnosis of congestive heart failure, left ventricular failure or a rheumatic valvulitis.

When a pleural effusion appears the diagnosis becomes increasingly difficult. One now has the complete picture of congestive failure. The pleural effusion is still to be attributed to systemic venous congestion of the parietal pleura. However it encroaches on the lung to such an extent that evidences of pulmonary congestion appear secondarily. The history of the appearance of ascites prior to the frank decompensation and the findings of a small heart without murmurs should point to the proper diagnosis. A cardiac arrhythmia also can be eliminated by the absence of a mitral stenosis.

If the compression of the heart is produced by a combination of constrictive adhesions and fluid, then the heart size will be increased. This will add to the diagnostic difficulties, but it will not make them insuperable.

In 1 of the cases herein reported the constrictive pericarditis was definitely secondary to tuberculosis. In the 2 others, both of which were operated upon, a strongly positive tuberculin test was obtained. However microscopical examination of the scar tissue revealed no evidence of tuberculosis.

Of the 2 patients operated upon 1 died. He survived the operation, but showed only mild improvement, and died several weeks later with symptoms typical of cardiac failure. Unfortunately autopsy was not obtained. This patient was 53 years old and had had severe symptoms for about 4 years. In going over the patients reported in the literature

the poor results, particularly as related to mortality were much more common in elderly patients. In fact, very few who were operated upon were as old as this patient. It seems obvious that considerable irreparable myocardial damage existed in this patient. As a matter of fact, the heart muscle as uncovered by excision of the scar was so cyanotic and friable that we considered it almost necrotic and feared spontaneous perforation. Heart muscle which was as unhealthy as this obviously could not regain much of its original function. We are, therefore strongly of the opinion that the mortality rate will be much lower in young people whose cardiac muscle is more apt to be reasonably well preserved. It is even possible that patients past the age of 50 should be operated upon only if they appear to be reasonably good operative risks.

Observations on vital capacity might be important in determining prognosis as far as fatality following operation is concerned. For example, the vital capacity of patient in Case 2 who died several weeks after operation was 1600 before abdominal paracentesis, and 1600 after paracentesis contrasted to a vital capacity of 4600 in Case 1 in which recovery following operation was satisfactory.

The authors wish to emphasize particularly that recovery may take place for at least a year following operation. For example, in Case 1 patient showed improvement for at least a year following the date of operation. In fact, at the end of 1 year his strength had not completely returned to normal although he was relatively free from symptoms. When last seen, which was almost exactly 2 years after operation, he stated that his strength had entirely returned, that he was free from symptoms, and working daily running a press.

#### SUMMARY

Undoubtedly innumerable cases of constrictive pericarditis are erroneously diagnosed as congestive heart failure, hepatic cirrhosis, etc., because of the similarity of symptoms to those of constrictive pericarditis. It is particularly important that this error be avoided because sufficient operative reports are now available to establish the fact that although

the mortality rate is high, the results otherwise are excellent. Perhaps the first symptom of constrictive pericarditis is weakness, followed soon by dyspnea upon exertion. Of great diagnostic significance is the fact that in this disease the dyspnea is not present while the patient is inactive and that ascites precedes edema of the extremities. Distended neck veins, high venous pressure, paradoxical pulse, and small cardiac shadow constitute important evidence for the diagnosis.

Since conservative treatment of the disease is hopeless, operation should be performed early, before myocardial damage due to compression, etc., is irreparable. Results are much better in young people, very few patients in late adult life survive the operation. Results may not be immediate, as emphasized by the fact that in one of our patients strength was still subnormal 1 year following operation, but 2 years after operation he felt perfectly normal and was working daily running a press.

# BIBLIOGRAPHY

1. BRECK, C. S. Surgical treatment of pericardial scar. *J. Am. M. Ass.*, 1931, 97, 524. Acute and chronic compression of heart. *Am. Heart J.*, 1937, 14, 515.
2. BIRWILL, C. S. and BLALOCK, A. Chronic constrictive pericarditis. *J. Am. M. Ass.*, 1938, 110, 265.
3. CHURCHILL, I. D. Decordication of the heart for adhesive pericarditis. *Arch. Surg.*, 1929, 10, 1457.
4. DELORENT, PROF. Sur un traitement chirurgical de la symphyse cardio-pericardique. *Bull. et Mém. Soc. d. chir.*, 1808, 74, 918.
5. HARRINGTON, S. W. and BARNES, A. R. Diagnosis and surgical treatment of chronic constrictive pericarditis. *South. Surg.*, 1940, 9, 459.
6. HATCH, G. J. and STEWART, H. J. The surgical treatment of chronic constrictive pericarditis. *Surg., Gynec. & Obst.*, 1930, 68, 979. Chronic constrictive pericarditis, dynamics of circulation and results of surgical treatment. *Arch. Int. Med.*, 1939, 63, 504.
7. KINS, J. Die perikardialen Verwachsungen im Kindesalter. *Arch. f. Kinderheilk.*, 1920, 68, 179.
8. SUMI, I. S. and LUCETT, H. S. Cardiolysis for chronic mediastinopericarditis. *Proc. Inter. State Post Grad. M. Ass. N. Am.* (1938), p. 489, 1929.
9. VOTHARD, PROF. and SCHMIDT, V. Behandlung der Einkammerung des Herzens durch schließliche Perikarditis. *Klin. Wchnschr.*, 1923, 2, 5.
10. WHITE, P. D. Chronic constrictive pericarditis treated by pericardial resection. *Lancet*, 1935, 2, 539. *Ibid.*, 1935, 2, 597.

# EXTENSIVE CUTANEOUS BURNS

With Special Reference to the Blood Chemical Changes

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THE historical background of burns has been adequately covered in many previous publications and need not be repeated; however, one quotation from the older literature seems pertinent:

From the very great variety of applications so strongly recommended by the first characters

biased individual would be at a loss on what to determine. I presume one of the great causes of error is the assuming that various applications the cure

of slight burns, some of which doubt could have got well without any and perhaps much sooner than with those which were used. This mistake frequently happens from good motives, and by the best intentioned people for if we have seen a person recover from any complaint during the use of any particular means, we naturally imagine such beneficial effect to have arisen from that cause although upon further investigation, it may be found to have been inadequate.

Thus, in 1797 Edward Kentish expressed his opinion of the contemporary investigation and treatment of burns. In the past 50 years many different local applications have been recommended likewise many theories have been presented to explain the cause of the systemic manifestations seen in burned patients.

No attempt has been made in this study to evaluate the various local applications. The feeling in this clinic has been that cleanliness is the most important factor in the local care of the burned area. The patients to be presented in this study were given adequate doses of morphine on admission; then, when comfortable and if the general condition permitted, the burned areas were washed with gauze sponges, soap and water while débridement was carried out at the same time. Most burns except those of the face and hands were covered with either a tannic acid silver nitrate (3) eschar or a gentian violet silver nitrate (5) eschar. Blair jelly was applied to

burns of the face and hands immediately after cleaning and after 48 hours, continuous saline soaks were applied.

Underhill and his associates (27) have shown that immediately after severe burns primary shock may develop as the result of pain and fright; they also stressed the importance of hemoconcentration resulting from plasma loss into the burned area, mainly during the first 24 hours (22, 23, 24, 26, 27). Aldrich has emphasized the rôle that absorption of bacterial toxins from an infected burned area may play in producing systemic changes. The time relationship between these three factors may be diagrammatically represented as shown in Figure 1. With adequate therapy these factors may be prevented or controlled, but even so the burned patient may still develop a syndrome characterized by lowered blood pressure, tachycardia, hyperpyrexia, anorexia, malaise, increasing lassitude, and later in severe cases, delirium, coma, and death. This condition which usually makes its appearance 24 to 72 hours after the burn is usually referred to as the toxemia of burns, or more preferable—the toxic stage of burns. The etiology of this syndrome has been the subject of much study and discussion, and the recent trend of interest in this respect has been in the field of blood electrolytes.

Underhill in 1923 (24) pointed out a decrease in serum chloides following severe burns. In 1926 Davidson (7) confirmed this and made a note of a chloride retention which he concluded must lie in the tissues. One year later Davidson (8) reported a study of serum proteins in which he found a slight decrease over a period of days after the burn, though frequently an increase was noted in the presence of hemoconcentration. Wiener, Rowlette, and Elman, in 1936 emphasized the fact that large amounts of parenteral saline solution frequently carries the serum protein to an

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edema level. All of these findings have since been confirmed by several groups of investigators (9, 14, 25), however, very few studies have been made on the effect of severe burns on potassium. Wilson (32) found a consistent, marked decrease in the serum sodium level corresponding with the general condition of the patient, treatment with desoxycorticosterone acetate tended to elevate the serum sodium with a coincident clinical improvement in the patient. Wilson also noted elevations of the serum potassium. Scudder (19) has presented a study of plasma potassium in 6 cases of severe burn in which he found elevations similar to those he had found in other forms of shock, he employed eschatin<sup>1</sup> in the treatment of these cases. Keeley, Gibson, and Pijoan carried out blood electrolyte studies on 7 dogs after experimental burning but found no increase in the serum potassium. This finding may possibly be explained on the fact that the potassium in the dog's red cells is very nearly the same as in the serum, thus, less potassium would be liberated after cell damage and intravascular hemolysis.

If one considers the known pathological physiology which follows severe burns, an elevation of plasma potassium would be predicted for several reasons: (a) the tissue autolysis, which follows death of cells after burning, necessarily sets free the intracellular potassium, (b) hemolysis of the red cells within the vessels of the burned area likewise liberates potassium, (c) in the presence of a low-

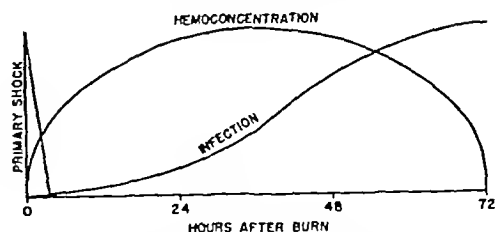


Fig 1 Showing the chronological relationship between primary shock, hemoconcentration, and systemic manifestations of infection (Modified from Gunn and Hillsman)

ered blood pressure renal excretion is diminished, thus hindering the elimination of excess potassium, (d) the renal damage which occasionally follows severe burns would have a similar effect, (e) liver damage frequently occurs, and this may interfere with the hepatic storage of excess potassium, and finally, (f) adrenal degeneration, infarction, and hemorrhage have all been described as occasional findings at autopsy, and in such cases sodium and potassium metabolism would certainly be effected.

It is the purpose of this study to evaluate the rôle of blood electrolyte changes, especially potassium, in the production of the symptoms of the toxic stage of burns.

#### METHOD OF STUDY

Eight cases of severe burn entering the Detroit Receiving Hospital were selected for study. There were 2 females and 6 males in this group, and the ages ranged from 8 to 51 years. The causes of injury were house fire, clothing on fire, and gas explosion. The

<sup>1</sup>Eschatin—adrenal cortical hormone manufactured by Parke Davis and Company

TABLE I—POSTMORTEM FINDINGS IN THE 3 FATAL CASES STUDIED

|                        | F B  | G B   | C R  |
|------------------------|--|---|--|
| Lungs                  | Extensive bronchopneumonia<br>Evidence of chronic congestion | Severe hyperemia                                    | Moderate hyperemia                                     |
| Heart                  | Normal   | Normal  | Coronary arteriosclerosis Grade I<br>Normal myocardium |
| Gastrointestinal tract | Normal   | Mild terminal diffuse hemorrhagic gastritis         | Normal   |
| Liver                  | Occasional areas of mild focal necrosis Grade I cirrhosis    | Mild parenchymatous degeneration                    | Occasional very small areas of mild focal necrosis     |
| Kidneys                | Normal   | Moderate hyperemia                                  | Moderate hyperemia Mild toxic nephrosis                |
| Spleen                 | Splenomegaly (970 gms.)<br>Primary splenic fibrosis          | Severe hyperemia with small areas of hemorrhage     | Moderate hyperemia                                     |
| Adrenal glands         | Very occasional area of focal necrosis                       | Enlarged (3 times) Cloudy swelling of cortical cell | Normal   |

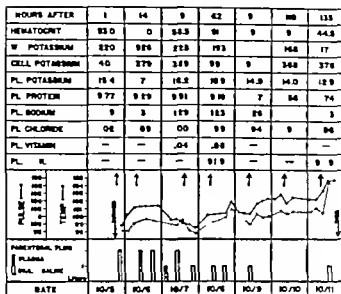


Table II—F B white, ♂ aged 47 5 per cent of body burned in gas explosion

depth of burn in each case was diagnosed as first, second, third, and fourth degree burns (Dupuytren's classification, 15) the smallest total area involved was 15 per cent and the largest 50 per cent of the total surface area of the body (Berkow scale)

Blood pressure studies could not be carried out on any of these cases as all of them were burned over both upper extremities. Evi-

dence that the toxic stage was present is based purely upon clinical judgment with the aid of the temperature and pulse charts. L. T. and O. C. showed no definite toxic symptoms. M. P. B. L. and W. P. showed moderate reactions but at no time were in shock. These 5 patients recovered. Unquestionable severe symptoms of the toxic stage were present from the second 24 hour period after burning until

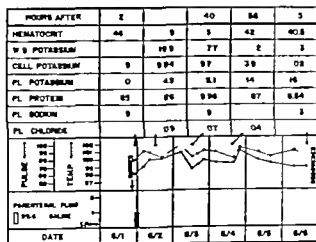


Table III—L T white, ♀ aged 35 5 per cent of body burned Clothes on fire.

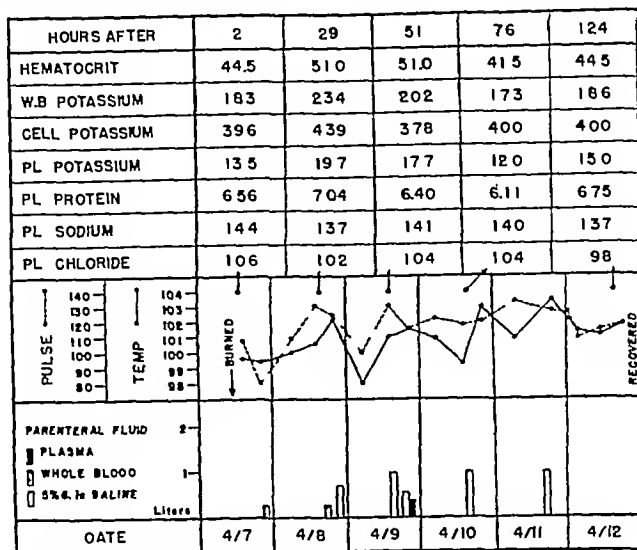


Table IV —B L, white, ♂, aged 11 years, 20 per cent of body burned. Clothes on fire

death in Cases F B, G B, and C R. At autopsy F B showed an extensive bronchopneumonia, probably as the result of inhaling hot fumes, however toxic symptoms were present for at least 3 days before the pneumonia developed. In Cases G B and C R no definite pathological cause of death could be found at autopsy. Table I shows the post-mortem findings in these 3 fatal cases.

Parenteral plasma, whole blood, glucose, and saline were given each patient as indicated. It is granted on retrospect that the treatment was not ideal in all cases, but it was sufficient to prevent primary shock, to control hemocoagulation, and to keep infection to a minimum.

All blood samples were taken at an interval when no parenteral fluid was being administered. Ten cubic-centimeters of venous blood were drawn into a clean syringe and carefully transferred to a tube containing 2 milligrams of dry purified heparin. The tube was then tipped four or five times in such manner that the heparin dissolved without causing foaming of the blood. Two cubic centimeters of blood were then immediately poured into another tube for hematocrit and whole blood potassium determinations, and the remainder of the blood was centrifuged without delay.

This extreme care and speed is necessary because of the great error in potassium determinations which can result from diffusion of potassium from cells to plasma or by liberation of cellular potassium through hemolysis. Heparinized plasma was chosen in preference to serum because a greater interface exists between clot and serum than between centrifuged cells and plasma—thus allowing a greater area for diffusion. No blood was taken

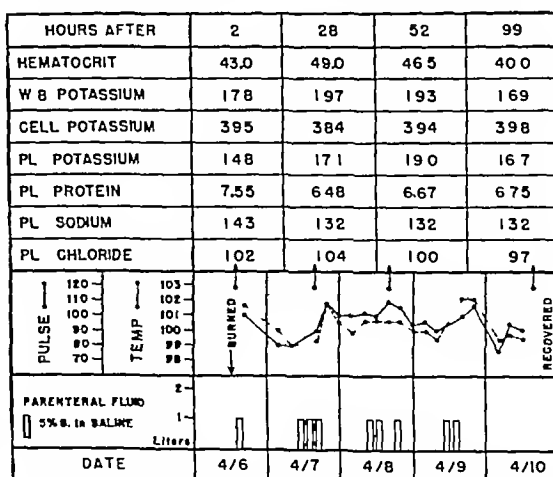


Table V —O C, negro, ♂, aged 51, 20 per cent of body burned. Clothes on fire



| HOURS AFTER    |      |      |      | 6    | 06  | 20 |
|----------------|------|------|------|------|-----|----|
| HEMATOCRIT     | 5.0  | 56.0 | 46.0 | 6    | 38  |    |
| W.B. POTASSIUM | 107  | 66   | 35   | 66   | 54  |    |
| CELL POTASSIUM | 408  |      | 367  | 06   | 679 |    |
| PL. POTASSIUM  | 6.8  |      | 5.2  |      | 6.6 |    |
| PL. PROTEIN    | 6.79 |      | 6.80 | 6.80 | 6.4 |    |
| PL. SODIUM     | 40   |      |      | 29   | 63  |    |
| PL. CHLORIDE   | 0    |      |      |      | 67  |    |

|                 |      |     |     |     |     |     |     |     |
|-----------------|------|-----|-----|-----|-----|-----|-----|-----|
| PERFUSION FLUID |      |     |     |     |     |     |     |     |
| DATE            | 3/31 | 4/1 | 4/2 | 4/3 | 4/4 | 4/5 | 4/6 | 4/7 |

Table VI.—M P Nic, ♀ aged 8, 20 per cent of body burned.  
House fire.

| HOURS AFTER    |      | 2    | 6    |      | 106 | 100  |
|----------------|------|------|------|------|-----|------|
| HEMATOCRIT     | 54.0 | 54.6 | 49   | 46.3 |     | 56.0 |
| W POTASSIUM    | 6    | 190  | 3    | 63   | 76  | 03   |
| CELL POTASSIUM | 66.0 | 3    | 0    | 37   |     |      |
| PL. POTASSIUM  | 6    | 6.3  | 6    |      | 3.3 | 15.3 |
| PL. PROTEIN    | 6.93 | 8.0  | 6.44 | 6.96 | 6.1 | 46   |
| PL. SODIUM     |      | 63   | 33   |      | 36  | 33   |
| PL. CHLORIDE   | 1.0  | 106  | 06   | 04   |     | 09   |

|                 |      |     |     |     |     |     |
|-----------------|------|-----|-----|-----|-----|-----|
| PERFUSION FLUID |      |     |     |     |     |     |
| PLASMA          |      |     |     |     |     |     |
| PL. SALINE      |      |     |     |     |     |     |
| DATE            | 3/31 | 4/1 | 4/2 | 4/3 | 4/4 | 4/5 |

Table VII.—W P Nic, aged 3, 5 per cent of body burned.  
House fire.

after death in Cases F B G B and C R. be cause of the immediate postmortem rise in potassium which Scudder (20) has demon- strated.

The hematocrit was determined by centri- fuging for 20 minutes at 2,000 revolutions per minute in Van Allen hematocrit tubes (28) and the micro-Kjeldahl method (16) was used for the estimation of plasma protein. Potas- sium was determined on plasma and whole blood by the photo-electric chloroplatinic

acid method of Tenery and Anderson. Cell potassium was calculated by the formula

$$\text{Cell potassium} = \left( \frac{\text{whole blood K} - \text{plasma K} \times \frac{100}{\text{hematocrit}}}{\frac{100}{\text{hematocrit}}} \right) \times \frac{100}{\text{hematocrit}}$$

The method of Hoffman and Osgood was used for plasma sodium and plasma chlorides were determined by the method of Wilson and Ball (30)

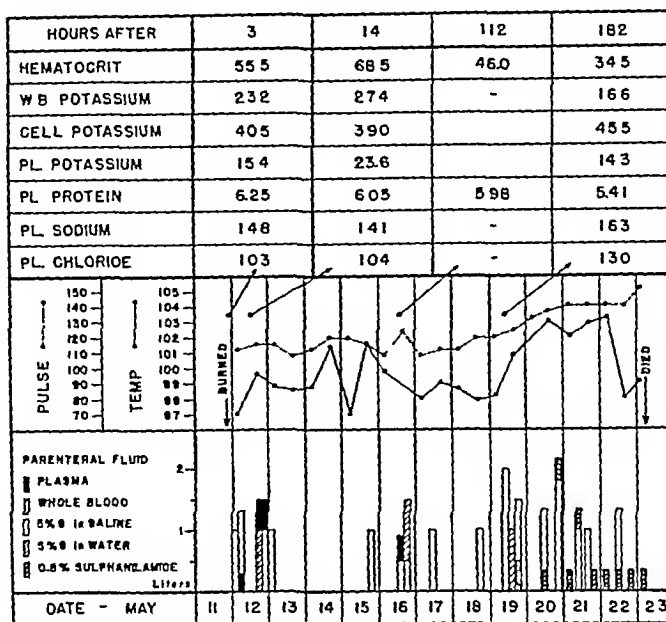


Table VIII —C R, white, ♂, aged 35, 40 per cent of body burned  
Gas explosion

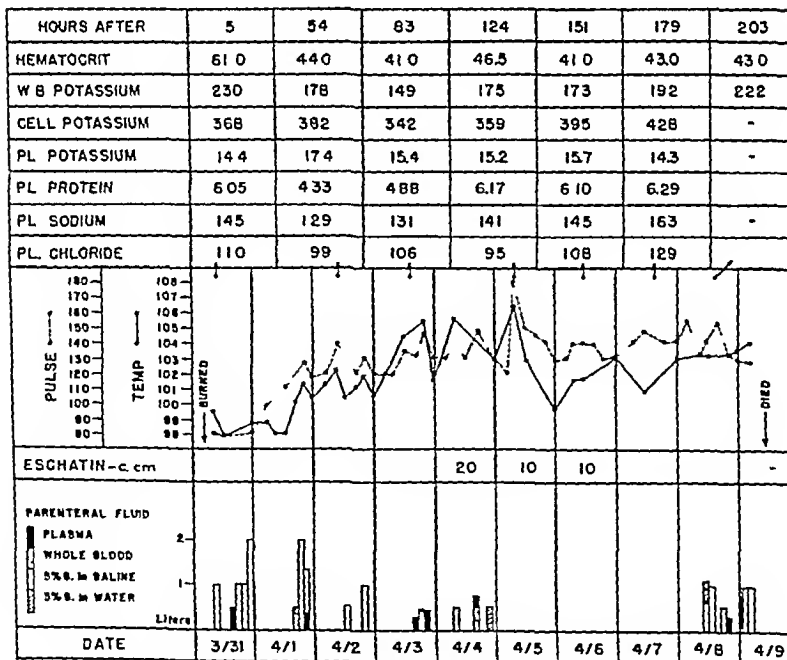


Table IX —G.B, white, ♂, aged 26, 50 per cent of body burned House fire

We have found an average normal range for each of these determinations to be hematocrit, 40 to 45 per cent cells, plasma potassium, 14 to 18 milligrams per 100 cubic centimeters whole blood potassium, 150 to 200 milligram per 100 cubic centimeters—depends on hema

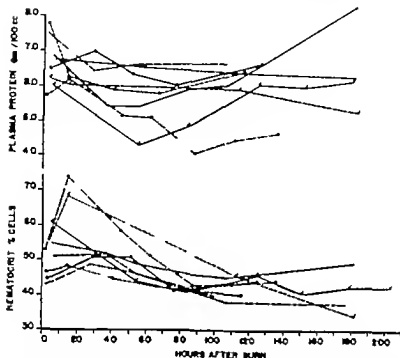


Fig. 2. Composite graph of plasma proteins and hematocrit on the 8 patients studied.

Key to Figs. 2, 3, 4.

— F.B.—W 47—5% body burned.  
 — L.T.—W 9 5—5% body burned.  
 — B.L.—W 8—10% body burned.  
 — O.C.—B 51—20% body burned.

— M.P.—W 9 8—20% body burned.  
 — W.P.—W 12—5% body burned.  
 — C.R.—W 35—20% body burned.  
 — G.B.—W 26—20% body burned.

tocrit cell potassium, probably 375 to 425 milligrams per 100 cubic centimeters plasma sodium 140 to 150 milli-equivalents per liter plasma chloride, 98 to 110 milli-equivalents per liter plasma protein 6.5 to 7.5 grams per 100 cubic centimeters.

#### FINDINGS

The results of these various procedures on the 8 patients studied are presented in Tables II to IX. The time relationships between the temperature, pulse, parenteral fluid, and blood chemical determinations are shown the small arrows at the top of each temperature chart indicate the time at which each blood sample was taken. Hematocrit is expressed as per cent of cells, potassium as milligrams per 100 cubic centimeters, and sodium and chlo-

ride as milli-equivalents per liter. Figures 2, 3 and 4 are composite graphs of the cases studied.

In all of these patients the hematocrit rose (Fig. 2) but only in C.R., G.B. and F.B. did it reach a very high level before adequate therapy brought about dilution. It was of great interest to note the relatively high readings of the first sample from each case though taken only a short time after burning. F.B. had a hematocrit of 53 per cent only 1 hour after receiving burns of 25 per cent of the body. In a patient, whose case is not reported in this series who had burns over 100 per cent of the body surface we found a reading of 71 per cent in venous blood 1 hour after burning; this would indicate that about one half of the total plasma volume had been lost

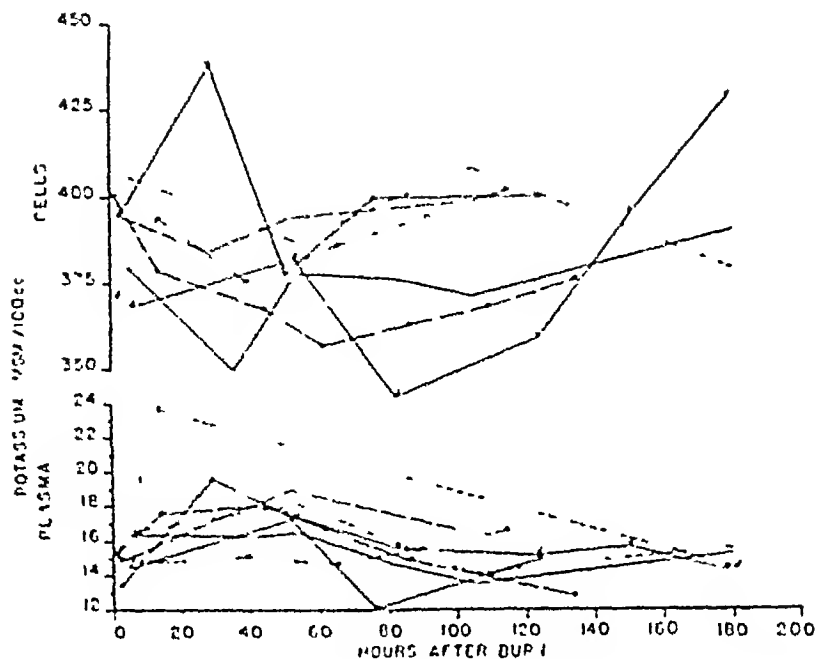


Fig. 3—Composite graph of plasma potassium and cells on the 8 patients studied.

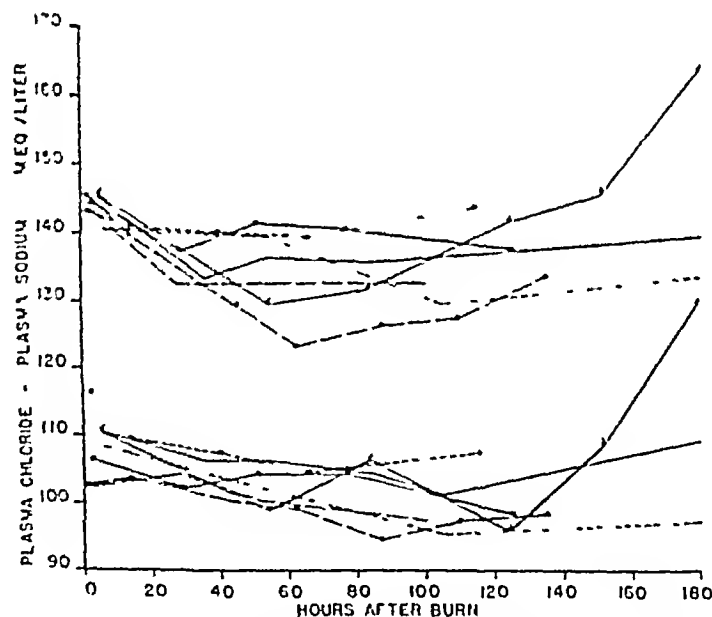


Fig. 4—Composite graph of plasma sodium and chloride on the 8 patients studied.

in that short time. In general, we have found that about one half of the hemoconcentration that is to occur was present 6 hours after the

burn. This indicates the need for plasma transfusion as early as possible as hemoconcentration is easier to prevent than relieve.

The plasma protein levels (Fig. 2) in these cases are similar to those previously reported. G. B. was given large amounts of saline and relatively little plasma in the first 54 hours after injury with a resultant marked drop in plasma protein accompanied by clinical edema. M. P. was given no parenteral saline and consequently had only a gradual slight lowering of the protein. The findings in all cases indicate the need for conservatism in the use of parenteral saline, and show a definite advantage in the use of plasma for preventing and relieving hemoconcentration.

Plasma potassium findings were rather disappointing (Fig. 3). Increases in the potassium level did occur in the first 48 hours in all patients except L. T. whose burns were the slightest; however in no case did the potassium reach a toxic level. It is quite probable that elevations would have been greater had the patients not received treatment, but the important point is that the toxic symptoms of burns were present without the presence of a toxic plasma potassium level.

Since the potassium content of cells is about twenty times greater than that of plasma, whole blood potassium varies almost directly with hematocrit changes and so means very little in itself.

The cell potassium is of interest though somewhat confusing (Fig. 3). The normal variation of potassium in the cells is rather inconstant; however in general a decrease occurred in most of the cases during the first 48 hours which was followed by a rise. Estimations of the cell hemoglobin content indicate that part of this decrease is the result of intracellular dilution; this may be further confirmation of the concept that the red cells become swollen in shock (6).

In spite of the relatively large amounts of parenteral saline the plasma chlorides consistently decreased slowly though in no case did this reach a dangerous level (Fig. 4). In contrast, the sodium level fell to a much greater degree. In M. C., F. B. and G. B. the plasma sodium dropped below 130 milliequivalents per liter. This could be a manifestation of adrenal insufficiency in spite of the normal plasma potassium because it has been shown that symptoms of Addison's dis-

ease can exist with a normal potassium if the sodium is low. G. B. was given eachatin; this was followed by a rise in the plasma sodium and chloride, but clinically the patient remained in circulatory failure and died.

C. R. showed a definite picture of burn toxemia without lowered plasma sodium and the remaining cases in general showed no relationship between the plasma sodium level and the presence of toxic symptoms. That sodium may play a large rôle in the morbidity of burned patients cannot be denied, and for their investigation is definitely indicated.

Plasma vitamin C determinations were carried out on F. B. Unfortunately the first sample was not taken until 45 hours after burning; at this time the level was 0.04 milligrams per 100 cubic centimeters. He was then given large doses of ascorbic acid by mouth, and 3 days later the level was 0.14. This man was an old alcoholic and so may well have had a vitamin deficiency before his accident; however it is interesting to speculate as to whether or not his injury had anything to do with his having such a very low level of vitamin C.

#### CONCLUSIONS

1. Primary shock, hemoconcentration and infection may all occur after extensive burns. With adequate therapy these can be controlled, but some patients will still show signs of the toxic stage of burns.

2. The data presented here indicate that under the usual mode of therapy (intravenous plasma and saline) the toxic symptoms may develop and cause death without marked changes in the blood electrolyte pattern. The exception to this may be sodium which is definitely lowered; however these data indicate no definite relationship between this drop and the clinical picture.

3. We do not imply that blood electrolyte changes are of no importance following burns; such changes must be carefully watched and controlled, otherwise the morbidity and mortality will be markedly increased.

4. Plasma is the ideal parenteral fluid to combat hemoconcentration and should be started within the first 6 hours after the burn is received.



The plasma protein levels (Fig. 2) in these cases are similar to those previously reported. G B was given large amounts of saline and relatively little plasma in the first 54 hours after injury with a resultant marked drop in plasma protein accompanied by clinical edema. M I was given no parenteral saline and consequently had only a gradual slight lowering of the protein. The findings in all cases indicate the need for conservatism in the use of parenteral saline, and show a definite advantage in the use of plasma for preventing and relieving hemoconcentration.

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# TENERY EXTENSIVE CUTANEOUS BURNS, BLOOD CHEMICAL CHANGES

5 Parenteral saline is essential after severe burns as a method to combat the tendency for plasma sodium and chloride to fall and perhaps to prevent elevation of plasma potassium, however, saline must be given judiciously because large amounts bring about a marked decrease of plasma protein, often to the edema level

6 The value of adrenal cortical hormone cannot be evaluated from our small experience with these preparations

7 The etiology of the toxic stage of burns is still unknown, the observations here presented indicate that blood electrolyte changes are not the answer Perhaps a toxin is produced in the burned area Wilson (31) has demonstrated the presence of a toxin which he believes is formed gradually by the autolysis of the injured tissue, and Rosenthal (17, 18) has found a histaminoid substance in burned tissue which is neutralized by serum from recovered cases of burn—neither of these concepts has been disproved

I wish to thank Dr Charles G Johnston and Dr J Logan Irvin for their aid and advice in this investigation I also wish to thank Dr O A Brines for his aid in the pathological interpretation of the autopsy material presented

## BIBLIOGRAPHY

- ALDRICH, R H The rôle of infection in burns with especial reference to gentian violet treatment *New England J Med*, 1933, 208 299-307
- BERKOW, S G A method of estimating extensiveness of lesions (burns and scalds) based on surface area proportions *Arch Surg*, 1924, 8 138-148
- BETTMAN, A G Tannic acid and silver nitrate in burns *Surg, Gynec. & Obst*, 1936, 62 458-463
- BLAIR, V P, BROWN, J B, and HAMM, W G The early care of burns and the repair of their defects *J Am M Ass*, 1932, 98 1355-1359
- BRANCH, H E Extensive burns, treatment with silver nitrate and methyl rosaniline *Arch Surg*, 1935, 35 478-485
- BRENNAN, H J Plasma transfusions in the treatment of hemorrhage *Brit. M J*, 1940, 1 1047-1048
- DAVIDSON, C C Sodium chloride metabolism in cutaneous burns and its possible significance for a rational therapy *Arch Surg*, 1926, 13 262-277
- Idem Plasma proteins in cutaneous burns *Arch Surg*, 1927, 15 265-274
- ELKINTON, J R, WOLFF, W A, and LEE, W E Plasma transfusion in the treatment of the fluid shift in severe burns *Ann Surg*, 1940, 112 150-157
- GUNN, JOHN, and HILLSMAN, J A Thermal burns *Ann Surg*, 1935, 102 429-443
- HOFFMAN, W S and OSGOOD, B A photoelectric method for the microdetermination of sodium in serum and urine by the uranyl zinc acetate precipitation *J Biol Chem*, 1938, 124 347-351
- KEELEY, J L, GIBSON, J G II, and PIJO, The effect of thermal trauma on blood volume, serum protein, and certain blood electrolytes: an experimental study of the effect of burns *Surg, Gynec. & Obst*, 1939, 5 872-893
- KENTISH, EDWARD An Essay on Burns Printed by G G & J Robinson, Paternoster-row, W London, 1797
- McCLURE, ROY D The treatment of the patient with severe burns *J Am M Ass*, 1939, 113 180-181
- PACK, G T The pathology of burns *Arch Pathol & Lab Med*, 1926, 1 767-805
- PREGL, FRITZ Quantitative Organic Analysis 3rd ed. Philadelphia P Blakiston's Son & Co, Inc, 1936
- ROSENTHAL, S R The toxin of burns *Ann Surg*, 1937, 106 111-117
- Idem Neutralization of histamine and burn toxin *Ann Surg*, 1937, 106 257-265
- SCUDDER, JOHN Shock Blood Studies as a Guide to Therapy Philadelphia J P Lippincott Co, 1936
- SCUDDER, J, CORCORAN, D R, and DREW, Studies in blood preservation, the serum protein of cadaver blood *Surg, Gynec. & Obst*, 1936, 62 48-50
- TENERY, R M, and ANDERSON, C E A photometric method for the microdetermination of potassium in blood plasma by the chloroplatinate precipitate *J Biol Chem*, 1940, 135 659-669
- UNDERHILL, F P Changes in the blood concentration of electrolytes in the treatment of extensive superficial burns *Ann Surg*, 1927, 86 840-841
- Idem The significance of anhydremia in extensive superficial burns *J Am M Ass*, 1930, 95 8-9
- UNDERHILL, F P, CARRINGTON, G L, KAPSINOW, R, and PACK, G T Blood concentration changes in extensive superficial burns and their significance for systemic treatment. *Arch Int Med*, 1930, 95 31-49
- UNDERHILL, F P, FISK, M E, and KAPSINOW, R The relationship of the blood chloride and sodium chlorides of edema fluid produced by a superficial burn *Am J Physiol*, 1930, 95 334-338
- UNDERHILL, F P, and KAPSINOW, R The toxin of burned skin *J Lab & Clin Med*, 1936, 16 823-830
- UNDERHILL, F P, KAPSINOW, R, and FISK, M E Studies on the mechanism of water exchange in the animal organism *Am J Physiol*, 1930, 95 314
- VAN ALLEN, C M An hematocrit method for the estimation of blood volume *J Lab & Clin Med*, 1925, 10 1027-1040
- WEINER, D O, ROWLETTE, A P, and ELKINTON, J R The significance of loss of serum protein in the treatment of severe burns *Proc Soc Exper Biol & Med*, 1936, 34 484-486
- WILSON, D W, and BALL, E G A study of the estimation of chloride in blood and serum *Chem*, 1928, 79 221-227
- WILSON, W C, JEFFREY, J S, ROXBURGH, and STEWART, C P Toxin formation in burned tissues *Brit J Surg*, 1937, 24 601-611
- WILSON, W C, and STEWART, C P Chemical changes in blood chemistry after burning injuries and the effect of grave surgical conditions, with some reference to treatment by desoxy corticosterone acetate *Brit J Surg*, 1930, 46 153-173



# POSTOPERATIVE INFECTION

## Measures of Control

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THE possible sources of contamination of the surgical field are many. Cole and Elman listed them as follows: (1) mouth and throat of the operating room personnel (2) skin of the surgeons and assistants' hands (3) patient's skin (4) faulty sterilization in autoclave (5) suture material chiefly catgut (6) gross break in aseptic technique (7) trauma to tissues, poor hemostasis, sutures under tension. To this one may add the fluctuations of immunity and changes in the virulence of bacteria, which may convert a subclinical unrecognizable contamination into a manifest, clinical infection.

The purpose of this discussion is to describe the methods utilized to minimize the dangers from the sources enumerated and to present statistical data based on the study of clean surgical wounds. All operations were performed at St. Luke's Hospital, Chicago, and some of the suggestions incorporated originated from members of the operating room committee and the surgical supervisors whose help is gratefully acknowledged.

### THE ELIMINATION OF SOURCES OF INFECTION

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12 minutes, with his mouth and nose masked with the customary gauze mask, 1,361 bacteria of the same kind were recovered per 10 cubic feet of air. He also showed that the permeability of the mask increased with time. In the first 2 minutes only 20 bacteria passed through, but the count increased with every 2 minute period and during the fifth 2 minutes 317 bacteria passed through per 10 cubic feet of air. Obviously the ordinary six ply gauze mask when worn for an hour or more is incapable of filtering bacteria. In hot weather the masks are often moist when removed and some surgeons even moisten the mask before use for cooling purposes. Such masks seem quite useless and one wonders whether Hertzler's contempt of masking the mouth or nose does not have some justification as far as the gauze mask is concerned. Gauze or calico masks containing rubber cellophane plastic, or any other impermeable material have not solved the problem. We have tried every one of these. It is true that the impermeable material incorporated into a pocket of the mask prevents a direct spray of bacteria into the wound but they simply deflect the bacterial current and the air of the operating room receives an unfiltered stream of bacteria. The air contamination of the operating room has recently received a great deal of emphasis and the 'deflector' type of masks certainly do nothing to minimize this source of contamination.

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The sterilization of the air in operating rooms, as approached with such vigor and ingenuity by Hart and his associates (13, 14, 15), is only a partial and certainly an indirect solution of the problem As long as it is generally admitted that the degree of air contamination in any room is directly proportional to the duration of occupancy, the number of occupants, the percentage of carriers and the intensity of the air pollution, effective masking seems to be the crux of the situation The elimination of the carriers has been tried in different services (Meleney, Hart) and has been found to be impracticable Cultures from the nose and throat change from day to day The training of student nurses is seriously hampered by their frequent and repeated elimination from the operating room, internes and attending men in a busy general hospital cannot be made to stop their work if their throat cultures become positive At St Luke's Hospital the attempt was made for a short period to eliminate all student and graduate nurses from the operating room and the maternity wards whose throat cultures were positive for hemolytic streptococci, the *Staphylococcus aureus* carriers were not included in this group Table 1 shows the result of throat cultures on a total of 99 student and graduate nurses over a 10-week period It is obvious from this greatly abbreviated report that in the fall of 1936, 20 per cent of the nursing staff connected with operating rooms or maternity wards carried hemolytic streptococci After a short period of elimination of the carriers the nursing school properly pointed out that as long as the attending and interne staff were not cultured the prophylactic value of such a measure was dubious, furthermore, the training of the student nurses was seriously hampered

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October 21, 1936—February 9, 1937

|                            | Cases |
|----------------------------|-------|
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| Positive on first culture  | 20    |
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Of the 6 positives on second culture 3 remained persistently positive 2 became intermittently negative, 1 remained persistently negative Of the negatives on first culture 3 became intermittently positive Cultures were taken once a week

In a personal communication Dr Frank Meleney stated that during the late winter and early spring months the incidence of positive throat cultures in the personnel amounted to a peak of 35 per cent, they still maintained (February 15, 1937) an elimination of the carriers for the Sloane Hospital as it was felt that on the maternity service the nurses come into much closer contact with the patients, particularly in the postpartum period

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# POSTOPERATIVE INFECTION

## Measures of Control

GEZA de TAAATS, M.D. F.A.C.S. and JOSEPH H. JESSER, M.D. Chicago, Illinois

THE possible sources of contamination of the surgical field are many. Cole and Elman listed them as follows: (1) mouth and throat of the operating room personnel (2) skin of the surgeons and assistants' hands (3) patient's skin (4) faulty sterilization in autoclave (5) suture material chiefly catgut (6) gross break in aseptic technique (7) trauma to tissues, poor hemostasis, sutures under tension. To this one may add the fluctuations of immunity and changes in the virulence of bacteria, which may convert a subclinical unrecognizable contamination into a manifest, clinical infection.

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piece of outing flannel bought on the market for 9 cents a yard.<sup>1</sup> It is inserted between two layers of a 44 by 40 thread mesh gauze. There is one thickness of this gauze on each side. An ordinary one half inch tape 44 inches long is sewn along the upper and lower border of the mask. Two 1 inch tucks are taken at the two sides of the mask, shortening their lengths to 4 inches and insuring a close fit over the cheeks. A pocket is left for the insertion of a flexible metal band for closer fit on the nose. The cost of the mask to the hospital, including material and labor is 5 cents. It can be re-sterilized many times.

2. *The skin of the surgeon and assistants hands.* The most revealing work on this subject has been that of Price. He recommended a soap and warm water scrub of the hands and forearms for 7 minutes, which rids the skin of gross dirt, fat transient bacteria, and approximately 50 per cent of the basic flora; this is followed by a 3 minute friction (by the clock) with 70 per cent (by weight) ethyl alcohol, which reduces the flora to less than 2 per cent. Ethyl alcohol, 70 per cent must be prepared by weight and not, as usually done by volume. Ethyl alcohol has a very narrow range of effective germicidal concentration. At 25 degrees Centigrade the following formula will give a solution approximately 70 per cent by weight: 95 per cent alcohol, 815 cubic centimeters, plus cold distilled water to make 1000 cubic centimeters. 60 per cent by weight approximately 70 per cent by volume is almost worthless. (23) Price pointed out that 1 minute contact with 70 per cent alcohol is equivalent to 4-5 minutes of scrubbing and also suggested a mixture of alcohols which is even more effective but which we have as yet not tried. Curiously enough the 7 minute scrub followed by 3 minutes immersion with friction (gauze or wash cloth) has been our method of skin preparation for many years.

Beneath the dry rubber glove the bacterial flora doubles in 40 minutes; hence glove punctures are dangerous. Devenish and Miles

emphasized the leakage of *Staphylococcus aureus* through glove punctures occurring during operation; such punctures occurred in 24 per cent of all cases and could be reduced to only 14 per cent in spite of eliminating patched gloves. They felt that the real danger of contamination with *Staphylococcus aureus* comes not from the nose and throat but from the skin of carriers leaking through the glove punctures or through the sleeves of linen gowns, moistened by sweat. Skin carriers could be best detected by culturing the sweat within the glove at the end of the operation. At our hospital one surgeon whose incidence of postoperative infection was unusually high was found to be such a carrier. According to Devenish and Miles a course of ultraviolet radiation had no effect on the skin of one of their carriers.<sup>1</sup>

3. *The skin of the patient.* Some of our surgeons have closely followed the routine advocated by Koch. Briefly his method is as follows: (1) careful soap and water cleansing with plain white soap of the field of operation on the afternoon preceding the operation. Protection of the cleansed field with a sterile dressing bladder or towel. (2) A second soap and water cleansing just before operation, for 10 minutes. The soapy solution is rinsed away with sterile water and the sterile draping is applied. No antiseptics are used.

We have followed this procedure for operations on the extremities or orthopedic work. For the majority of patients, however our choice is still an iodine-alcohol preparation. With the exception of an occasional case of iodine sensitivity of which the patient is usually aware we have not experienced the much discussed iodine dermatitis. It is essential, however to apply the 5 per cent tincture of iodine once, carefully to remove the excess with alcohol and then to apply a third dry swab the remaining iodine and alcohol being wiped off. The edges of the prepared field which are covered by sterile towels, are carefully wiped off. Trickling of the tincture of iodine into genitorectal areas or to the back of the patient is avoided. We have returned to the iodine-alcohol preparation after a thorough

Many believe that some backwash of mercury on hands that will tolerate it, following alcohol, an added safeguard.

<sup>1</sup>The types of Caesarean Section which serve as effective bacterial flora have been given to us by Dr. C. J. McKelvey at Cedarville, Devenish 27, 44 and Edwards 27, 25. We gratefully acknowledge Dr. McKelvey's help. Study of these works is being continued. Of course credited by Dr. McKelvey of our resident staff, the use as present use proved to be most efficient.

trial of the mercuric-chloride-acetone-alcohol mixture of Arnold, of mercurochrome, mer cresin and metaphen. While in a large general hospital, such as ours, every surgeon has his own favorite method, a gradual return to iodine is noticeable. A 2 per cent iodine solution in 70 per cent (by weight) of alcohol has been advocated by Price. It is inexpensive and has an important quality which test tube experiments for antiseptic coefficients will never demonstrate, i e., it produces a reactive hyperemia of the skin, which we have demonstrated with measurements of skin temperature, this together with a local leucocytosis is an excellent adjunct to primary union. For certain regions of the body, such as the genital, anal, and axillary regions, a 3 per cent aqueous solution of iodine has been employed with lack of iodine dermatitis, provided the field is carefully wiped off with a dry sponge.

The fingering of the prepared skin with the gloved hand to outline the line of incision is inconsistent with the customary efforts to cover the incised skin with towels and isolate the wound with towel clips. If preliminary marking of the line of incision is desired, we advocate the use of a two per cent solution of brilliant green applied before the iodine-alcohol preparation. Mercurochrome and metaphen solutions efface the brilliant green mark.

4 *Faulty sterilization in autoclaves* This subject was reviewed by Dandy in 1932. He advocated sterilization in an autoclave for one hour with a constant pressure of not less than 20 pounds. Meleney stated that sterilization for 30 to 45 minutes and prolonging the evacuation time at minus 10 to 15 minutes was sufficient to kill organisms and spores. With less time and pressure the center of the central drum may remain contaminated. At St. Luke's Hospital, 18 pounds of pressure are used for 1 hour followed by another hour of vacuum. A temperature of 250 degrees F is obtained.

5 *Suture material* The whole subject of catgut versus silk (11, 12, 17, 25, 31) and the recent work of Meade and Ochsner with cotton cannot be entered here. We simply wish to present our own procedure, learned in the schools of Kocher and developed in this country by Halsted. We use silk, and as fine

a silk as possible, unless some definite contraindication exists. The silk is usually interrupted, the peritoneum is closed with a continuous catgut suture and catgut is used in entero-anastomoses for the suture of the mucosa. Infection is not a contraindication to silk, and we have repeatedly tied large vessels with heavy silk or even tape in the presence of infection. We believe that the steady use of catgut increases the incidence of infections not only because the sterilization of catgut is not as simple but mainly because catgut produces local areas of exudation, and collections of serum predispose to infection. It must be admitted, however, that if catgut were used in such fine varieties as silk is, the difference between the true materials might not be so striking (17). If cotton continues to be as successful as the first reports indicate (21), we may look for a further improvement in suture material. It has been tried on our service in over 100 major operations.

6 *Gross break in aseptic technique* In large hospitals with student nurses and internes rotating every 6 weeks in the operating room, with a large surgical staff whose training is not always of identical nature, a break in asepsis has to be continuously guarded against. Visitors should always wear sterile caps, gowns, and have their mouths and noses covered. Visitors in nonsterile gowns when they lean against the drapings or the exposed backs and elbows of the surgical team are a definite menace. The dripping of perspiration from the foreheads of the surgeons and assistants is a frequent source of danger. We have tried some of the sponge-mops which are on the market, but their wear is cumbersome and may increase perspiration. While air conditioned operating rooms eliminate much of the perspiration, large blocks of ice placed in front of a fan have been tried, their use may be objected to as they stir up dust in the operating room and facilitate the migration of bacteria toward the wound.

A frequent source of a sudden spray of dust and bacteria is the sudden shifting of the lighting system directly over the field of operation. When such a shift becomes necessary it is wise to cover the field with a sheet during this maneuver.

7 *Trauma to tissues poor hemostasis in tubes under tension* One hardly needs to be labor the point that rough handling of tissues, insufficient hemostasis, sutures under tension which invite localized areas of ischemia, favor the multiplication of ever present bacteria. It is less often realized that foci elsewhere in the body may be stirred up by the trauma of the operation and anesthesia and bacteria may then localize in the surgical field. This is particularly true of acute respiratory infections. During an influenza epidemic in a large base hospital, one of us observed the suppuration of many clean wounds that had been healing without reaction for 5 to 7 days. When the epidemic hit the clean surgical ward a large percentage of the wounds became infected with bacteria which are secondary invaders following the virus, namely, the *Streptococcus hemolyticus*, and the *Staphylococcus hemolyticus*. A patient, then, should never be operated on except in emergencies when a respiratory infection is present not only because of the danger of postoperative pulmonary complications but because of the possible localization of bacteria in the surgical field. The classic experiment of producing a localized abscess at the site of trauma following an intravenous injection of bacterial suspension is sufficiently known, but its application to the localizing effect of surgical trauma is often ignored.

8 *Other sources of infection.* Another source of infection in postoperative wounds is the presence of bacteria in a latent "resting" state in the tissues. This problem in its relation to the activation of phlebitis in varicose veins has been discussed elsewhere (8). The principle of activating resting infection by surgical trauma and especially by creating anaerobic or partially anaerobic conditions has an important application in all surgical operations where potentially infected fields are invaded. Gas gangrene following amputations for vascular disease is an example (9). The torn or overstretched muscle of a muscle splitting incision may be of more harm to the patient than a clean, sharp cut in the muscle, provided it does not damage its nerve supply.

That more infection does not result from such endogenous sources is no doubt due to the patient's immunity. This immunity may

be local developing around a chronic anal fistula, or general. But the immunity of patients to specific bacteria varies from day to day. Schafer found that in the months of January and February immunity of animals is at its ebb for diphtheria. Epidemics of scarlet fever are explainable not by the sudden appearance or multiplication of bacteria but by a sudden decrease of immunity. The sudden overwhelming septicemia following clean operations, which, according to Hunt, occurs in 1 of 2000 to 3000 cases may be explained in the absence of any recognizable source of infection by such a sudden loss of immunity.

Mrs. D. T. A 4 year old rather obese woman had a small epigastric hernia which was repaired under local anesthesia. An all-silk technique was used. The operation lasted 35 minutes. On the night of the operation the patient had a severe chill, 101.4 hours she died of fulminating septicemia. Hemolytic streptococci were cultured from the blood, the spleen, and other organs. The field of the operation showed no infection. All possible sources of infection were checked. Throat cultures of the operating room personnel were negative. The procaine solution was sterile. The silk, as usual, was sterilized with instruments in boiling water for 15 min. The patient's throat was slightly infected unfortunately. Culture was made from it.

Such a case, which may occur in the practice of any surgeon, illustrates the difficulty of detecting some sources of infection or preventing their occurrence.

#### MATERIAL STUDIED

The purpose of our present study was to see what results were obtained with the methods here outlined, to emphasize the weak points, and if possible, suggest their remedy. The material to be presented illustrates the results obtained in a general hospital in which yearly over 7,000 major operations are performed. As some of the special sheets were incompletely filled out, we can present data on only 606 clean operations. An infection sheet was attached during the year of 1935 to the hospital record of every major surgical case. The classification of postoperative infections is that of Claude Beck as reported by William C. Beck in his recent survey on morbidity caused by operative complications (Table 11). For a check on our operating room technique we could utilize only the first

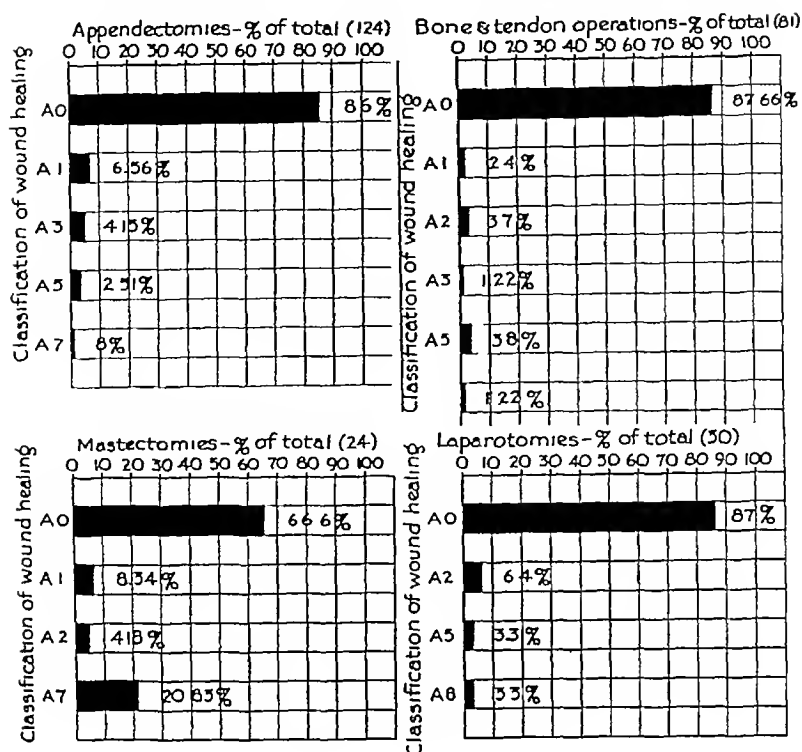


Chart 3 Wound healing classification

tomies and orthopedic operations, the lowest percentages were encountered following hysterectomies and mastectomies. Reddened skin edges were encountered in 20.3 per cent following hysterectomies and only in 2.4 per cent after orthopedic operations. Stitch abscesses, A<sub>2</sub>, were seen most often after laparotomies and least frequently after herniotomies. Slight serous or purulent discharge was seen most frequently after appendectomies, indicating the necessity of careful protection of the abdominal wall from contamination and the occasional use of drainage or delayed closure as advocated by Coller and Volk. Hematomas were most frequent after thyroidectomies, which, of course, is due to the nature of the operation. We have commented on the large percentage of skin necrosis following mastectomies.

#### EVALUATION OF RESULTS

The difficulties in evaluating the results of such a survey are obvious. In a general

hospital, the technique of different services and of individual surgeons varies. There were, of course, certain nonvariables, such as (1) the sterilization of instruments, suture material and surgical linen, and (2) the new air-filtering masks, which we do believe have an important rôle in diminishing air borne infection. The incidence of stitch abscesses, slight and serious wound infections, infected hematomas and septicemia totals 3.81 per cent of all clean operations, a truly excellent record compared with other carefully conducted surveys (22). On the basis of some experience with trying to establish the incidence of surgical infections from the ordinary hospital records, we have to come to the conclusion that aside from being a cumbersome and lengthy task, many minor infections are unrecorded and perhaps never known to anyone but the interne removing the stitches. We believe that in order to get comparative results, similar record sheets would have to be used by all institutions really interested in their per-



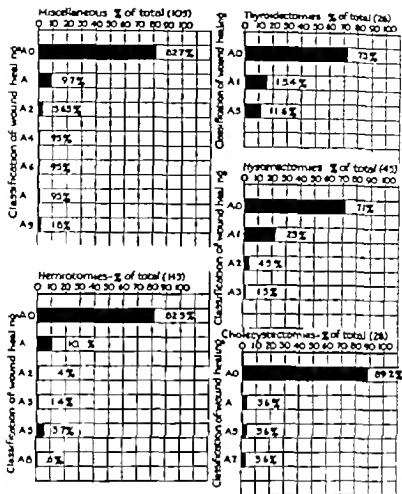


Chart - Wound healing classification.

of the record by the resident on gynecology or to the difficulty of sterilizing the field is uncertain. This service has since cut down the percentage to a small minimum. Cholecystectomies show a very high percentage of primary wound healing—89.2 percentage. In this hospital drainage is used in all cases for 2 to 4 days. In a miscellaneous group including neurosurgical cases, vascular surgery plastic surgery thoracic and genito-urinary patients, wound healing compared favorably with most other groups, owing perhaps to the special preoperative care of these patients.

Appendectomies did equally well with the exception of minor skin infections (Chart 3). The statistics on bone and tendon operations

are favorable especially in regard to the low incidence of minor skin infections and of hematoma. Following mastectomies, necrosis of the skin edges seemed to be a complication too often encountered. This is obviously due to the effort of removing as much skin as possible or saving too much undermined skin and may point to a more frequent use of immediate or delayed skin grafts. Other laparotomies behaved much like the average group.

When the operative procedures are grouped according to the postoperative reaction, the points mentioned obtain renewed emphasis (Chart 4). Primary union, A<sub>0</sub>, showed the highest percentage following cholecystec-

mum of infection following clean cases. We will have to pay more attention to the sterilization of the skin and to glove punctures. We are not in a position to evaluate the bactericidal effect of radiant energy on the contamination of the air in the operating room, but it is our feeling that the use of effective air filters in closely fitting masks is another step in the same direction, certainly a simpler one. Perhaps the mouth and pharynx of the operating room personnel could be temporarily sterilized with tablets or trochees, but there is no good evidence yet that this is practicable.

The fluctuations of immunity and their relation to sudden overwhelming infection is another open question, only slight use has been made in this hospital of the prophylactic doses of sulfanilamide before operations that readily lead to contamination from within the body, such as intestinal resections.

Whether the contamination with *Staphylococcus aureus* comes from the nose and throat of the personnel in the operating room (13, 14) or whether it is skin contamination (10) is impossible to decide. In an excellent review of the problem of air contamination, Walters and Magath lean toward the view that air contamination through respiratory passages and its effective sterilization by radiant energy is far from being proved. Certain it is that expensive and complicated ultraviolet radiation in operating rooms is still in the experimental stage and need not as yet burden the budget of the average general hospital.

#### SUMMARY

1. The sources of contamination of the surgical field have been discussed. The use of a new flannel mask has been described which efficiently filters bacteria but does not deflect them. The sterilization of the skin of the patient with soap and water, followed by iodine and 70 per cent alcohol, is advocated. Measures have been suggested which seal the suture line following operation. Silk was preferred to catgut.

2. Following the classification of Claude Beck, 606 clean operations have been studied in regard to their postoperative wound reaction. Postoperative infection resulting in prolonged stay in the hospital or danger to

life occurred in 1.59 per cent. A total of 3.81 per cent of all clean operations showed wound infection. Special interest has been focused on reddened skin edges as evidence of inadequate sterilization of the skin. Hematoma and marginal necrosis occurred more frequently in certain types of operations. The material was studied according to operative procedures and plotted against the different grades and types of delayed union.

3. The study is intended to stimulate similar efforts of record keeping in other hospitals. As a result of our own survey, further improvement in our records has already taken place. The filling out of the record is simple, not time consuming, and should be entrusted to the resident.

#### BIBLIOGRAPHY

1. ARNOLD, L. A new surgical mask. *Arch Surg*, 1938, 37, 1008.
2. BECK, W. C. Morbidity caused by operative complications. *Arch Surg*, 1939, 39, 478.
3. BLATT, M. C., and DALE, M. L. A bacteriological study of the efficiency of face masks. *Surg, Gynec & Obst*, 1933, 57, 363.
4. COLE, W. H., and ELMAN, R. *Textbook of Surgery*. New York and London: D Appleton Century Co., Inc., 1936.
5. COLLIER, F. A., and VOLK, W. L. Delayed closure of contaminated wounds. *Ann Surg*, 1940, 112, 256.
6. DANDY, W. E. The importance of more adequate sterilization processes in hospitals. *Bull Am Coll Surgeons*, 1932, 16, 11.
7. DAVIS, J. S. The importance of adequate masking during operations. *Ann Surg*, 1934, 100, 1008.
8. DE TAKATS, G. Resting infection in varicose veins. *Am J M Sc*, 1932, 134, 57.
9. DE TAKATS, G., and REYNOLDS, J. T. Amputation for peripheral vascular disease. *Arch Surg*, 1940, 40, 253.
10. DEVENISH, E. A., and MILES, A. A. Control of *Staphylococcus aureus* in an operating theater. *Lancet*, 1939, 1, 1088.
11. ELKIN, D. C. Wound infection. *Ann Surg*, 1940, 112, 280.
12. HALSTED, W. S. Ligature and suture material, employment of fine silk in preference to catgut. *J Am M Ass*, 1913, 60, 1119.
13. HART, D. Sterilization of the air in the operating room by special bactericidal radiant energy. *J Thoracic Surg*, 1936, 6, 45.
14. Idem. Sterilization of the air in the operating room by bactericidal radiant energy. *Surgery*, 1937, 1, 770.
15. HART, D., and SCHIEBEL, H. M. The rôle of the respiratory tract in contamination of air, a comparative study. *Arch Surg*, 1939, 38, 788.
16. HERTZLER, A. E. *The Horse and Buggy Doctor*. New York: Harper Bros., 1938.
17. HOWES, E. L. The strength of wounds sutured with catgut and silk. *Surg, Gynec & Obst*, 1933, 37, 309.

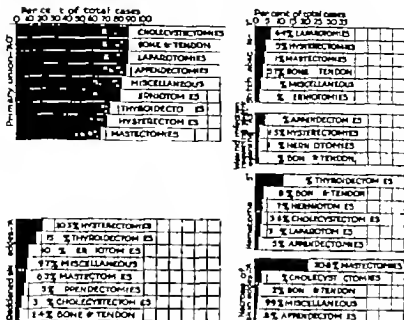


Chart 4. Operative procedures grouped according to wound healing.

centage of disturbed or delayed wound healing. The survey of William C. Beck offers a standardization of such studies.

The reddened skin edges are undoubtedly due to inadequate sterilization of the skin or a postoperative contamination of the wound. The gynecological service, on which 1 per cent mercurochrome was used, had the highest incidence. The highest and lowest percentages were 20.3 per cent and 2.4 per cent. In addition to the soap and water iodine and alcohol preparation we advocate two other measures to prevent delayed contamination of the skin after it has been sutured. One is the use of silverfoam under which we have never seen a true cutaneous infection; the other is the gluing of the gauze dressing to the skin with mastisol<sup>1</sup> which one of us (G. de T.) has been using since 1915 and which makes excellent small dressings for aseptic wounds. The importance of late skin infections is best seen in the many ambulatory vein ligations. In the hot summer months, where perspiration can readily increase the incidence of bacteria around the suture line, reddened skin

edges are far more frequently encountered. In over a thousand ambulatory vein ligations, which are not included here, mastisol was used but no silver foil or antiseptic dusting powder has been employed. During the hot spell of July, 1940, we became convinced, however, that ambulatory patients, especially require added care for the protection of the suture line from cutaneous bacteria. The pubic area is especially prone to minor skin infection, which may explain the high incidence after hysterectomies and inguinal hernias.

The results obtained here are readily surpassed by the individual surgeon who is especially conscious of postoperative infections. In surveying the practice of other hospitals one surgeon stated that "postoperative infection has occurred so infrequently that we have almost stopped thinking about it. This may be true of some surgeons of our institution. We were really interested, however, in determining the chances that the average patient has of developing an infection when operated on at St. Luke's Hospital. We have used rigid criteria for the establishment of the data published here.

It seems as if there is an irreducible mini-

<sup>1</sup>One mastisol 40 grams, iodine, and 200 grains. Filter then add gauze 22-24 centimeter x 1.

mum of infection following clean cases. We will have to pay more attention to the sterilization of the skin and to glove punctures. We are not in a position to evaluate the bactericidal effect of radiant energy on the contamination of the air in the operating room, but it is our feeling that the use of effective air filters in closely fitting masks is another step in the same direction, certainly a simpler one. Perhaps the mouth and pharynx of the operating room personnel could be temporarily sterilized with tablets or troches, but there is no good evidence yet that this is practicable.

The fluctuations of immunity and their relation to sudden overwhelming infection is another open question, only slight use has been made in this hospital of the prophylactic doses of sulfanilamide before operations that readily lead to contamination from within the body, such as intestinal resections.

Whether the contamination with *Staphylococcus aureus* comes from the nose and throat of the personnel in the operating room (13, 14) or whether it is skin contamination (10) is impossible to decide. In an excellent review of the problem of air contamination, Walters and Magath lean toward the view that air contamination through respiratory passages and its effective sterilization by radiant energy is far from being proved. Certain it is that expensive and complicated ultraviolet radiation in operating rooms is still in the experimental stage and need not as yet burden the budget of the average general hospital.

#### SUMMARY

1. The sources of contamination of the surgical field have been discussed. The use of a new flannel mask has been described which efficiently filters bacteria but does not deflect them. The sterilization of the skin of the patient with soap and water, followed by iodine and 70 per cent alcohol, is advocated. Measures have been suggested which seal the suture line following operation. Silk was preferred to catgut.

2. Following the classification of Claude Beck, 606 clean operations have been studied in regard to their postoperative wound reaction. Postoperative infection resulting in prolonged stay in the hospital or danger to

life occurred in 1.59 per cent. A total of 3.81 per cent of all clean operations showed wound infection. Special interest has been focused on reddened skin edges as evidence of inadequate sterilization of the skin. Hematoma and marginal necrosis occurred more frequently in certain types of operations. The material was studied according to operative procedures and plotted against the different grades and types of delayed union.

3. The study is intended to stimulate similar efforts of record keeping in other hospitals. As a result of our own survey, further improvement in our records has already taken place. The filling out of the record is simple, not time consuming, and should be entrusted to the resident.

#### BIBLIOGRAPHY

1. ARNOLD, L. A new surgical mask. *Arch Surg*, 1938, 37, 1008.
2. BECK, W. C. Morbidity caused by operative complications. *Arch Surg*, 1939, 39, 478.
3. BLATT, M. C., and DALE, M. L. A bacteriological study of the efficiency of face masks. *Surg, Gynec & Obst*, 1933, 57, 363.
4. COLE, W. H., and ELMAN, R. *Textbook of Surgery*. New York and London: D. Appleton Century Co., Inc., 1936.
5. COLLIER, F. A., and VOLK, W. L. Delayed closure of contaminated wounds. *Ann Surg*, 1940, 112, 256.
6. DANDY, W. E. The importance of more adequate sterilization processes in hospitals. *Bull Am Coll Surgeons*, 1932, 16, 11.
7. DAVIS, J. S. The importance of adequate masking during operations. *Ann Surg*, 1934, 100, 1008.
8. DE TAKATS, G. Resting infection in varicose veins. *Am J M Sc*, 1932, 134, 57.
9. DE TAKATS, G., and REYNOLDS, J. T. Amputation for peripheral vascular disease. *Arch Surg*, 1940, 40, 253.
10. DEVENISH, E. A., and MILES, A. A. Control of *Staphylococcus aureus* in an operating theater. *Lancet*, 1939, 1, 1088.
11. ELKIN, D. C. Wound infection. *Ann Surg*, 1940, 112, 280.
12. HALSTED, W. S. Ligature and suture material, employment of fine silk in preference to catgut. *J Am M Ass*, 1913, 60, 1119.
13. HART, D. Sterilization of the air in the operating room by special bactericidal radiant energy. *J Thoracic Surg*, 1936, 6, 45.
14. Idem. Sterilization of the air in the operating room by bactericidal radiant energy. *Surgery*, 1937, 1, 770.
15. HART, D., and SCHIEBEL, H. M. The rôle of the respiratory tract in contamination of air, a comparative study. *Arch Surg*, 1939, 38, 788.
16. HERTZLER, A. E. *The Horse and Buggy Doctor*. New York: Harper Bros., 1938.
17. HOWES, E. L. The strength of wounds sutured with catgut and silk. *Surg, Gynec & Obst*, 1933, 37, 309.

8. HERTZ E. L. Some further observations upon contamination of operative wounds by airborne bacteria. *New England J Med* 933, 800-93.
9. KOCK, S. L. Lacerations of the hand. *J Am. M. Ass* 934, 97-944.
10. M. KRAMER, C. F. STROGER, A. and LONG, A. P. Hospital infections. *Am. J Dis Child* 934, 55-579.
11. MEADE, W. H., and OGDONER, A. The relative value of catgut, silk, linen and cotton as suture materials. *Surgery* 940, 7-455.
12. MELENEY F. L. Infection in clean operative wounds. *Surg. Gynec. & Obst.* 935, 60-204.
13. PRICE, P. B. New studies in surgical bacteriology and surgical technique. *J Am. M. Ass* 938, 903.
14. SCHWARTZ, W. Arbeiten aus dem Staatshospital für exp. Therapie, No. 3 p. 5. Frankfurt, 935.
15. SMITHSON, P. The silk technique. *Surgery* 940, 7-9.
16. VARCHALL, J. A. and ARNOLD, L. Compounded solution of mercuric chloride for skin disinfection. *Surg. Gynec. & Obst.* 935, 6-333.
17. WALKER, J. S. How can we determine the efficiency of surgical masks. *Surg. Gynec. & Obst.* 935, 30-266.
18. WALTERS, W. W., and MAGATH, T. B. Operative and postoperative infections (with special reference to airborne bacterial contamination). *Ann. Surg.* 930, 27.
19. WATERS, E. G. Adequate surgical masking problem and solution. *Am. J. Surg.* 934, 5-474.
20. WELLS, W. P. On airborne infection. Apparatus for the study of the bacterial behavior of air. *Am. J. Public Health* 933, 3-38.
21. WHITFIELD, A. D. Use of silk in the repair of clean wounds. *Ann. Surg.* 933, 98-66.





Fig. 1. Photograph of ruptured primary ovum pregnancy. Dissected ovary measured 5.5 by 4.5 by 6 centimeter.



Fig. 2. Photograph of portion of dissected ovary revealing fetus attached by blood clots and membranes. 3. Photography by Clarence B. M. Bell.

Uterine Pregnancy. Ovarian Pregnancy. — Arthur H. Curtis







Fig. 3 Photomicrograph of ovarian villi. Chorionic villi, deeply staining syncytial cells and clear Langhans cells.

note that the pregnancy occurred in a patient in whom there was a veritable toboggan slide from the fallopian tube to the ovary. Just as fertilization of the ovum in the tube is a preliminary stage in the everyday occurrence and development of normal intra-uterine gestation, likewise it should be possible for the impregnated ovum to slide downward into the gaping recently ruptured ovary, there to develop. Whether an endometrial implant must furnish a favorable site for nidation of the ovum as was possible in this patient with endometriosis, is an additional problem, mention of which may suffice here.

Nearly 60 cases of primary or "true" ovarian pregnancy have been recorded in the literature of this number only approximately 60 are authentic instances of primary ovarian gestation. Despite the fact that only a small number of cases are recorded in the literature and many of these can-

not be accepted as authentic primary ovarian pregnancy is probably not at all rare and it very likely explains a considerable proportion of the cases of serious hemorrhage from the ovary also, it doubtless accounts for some instances of secondary abdominal pregnancy—a much more common affection than has heretofore been realized. (Lull has had 5 cases of abdominal pregnancy in his own practice.)

#### CONCLUSION

1. A case of living unruptured primary ovarian pregnancy has been described.

2. Evidence has been submitted in substantiation of the thesis that primary ovarian pregnancy may occur after fertilization in the fallopian tube just as normal intra-uterine gestation develops after fertilization in the fallopian tube. The belief that primary ovarian pregnancy occurs solely after fertilization of the ovum before its escape from the ovary is unwarranted.

3. Despite the fact that only a small number of cases of primary ovarian pregnancy are recorded in the literature and a considerable proportion of these are not authentic, it would appear that ovarian pregnancy often escapes recognition and it is always to be considered in cases of ovarian hemorrhage which are serious enough to require surgical intervention.

#### REFERENCES

1. LUDWIG, G. Beiträge zur Gynäkologie extruterin. I. Graafisches Internitium. Graviditas auf der Fimbria ovarica bei Plica Intendibulo-ovaria; Graviditas ovarialis. Arch. f. Gynæk., 1899, 53: 596.
2. SPRENGEL, G. Zur Klinik der Ovarialschwangerschaft. Arch. f. Gynæk., 1878, 3: 72.

# THE DISRUPTION OF ABDOMINAL WOUNDS

## A Continuation of a Previous Report

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**O**VER 3 years ago we reported 22 cases of disruption of abdominal wounds (1) occurring in a series of 2,927 patients on the surgical service of the New York Hospital during a period of 3 years and 8 months. Since the mortality of this serious complication continues to be from 22 to 50 per cent in various reported series we have again reviewed our experience with an additional 3,490 cases and consider in this study, therefore, a total of 6,417 abdominal wounds. From the data collected in the study of the first series of 2,927 patients certain conclusions were drawn leading to the application of general policies in the second series of 3,490 patients treated over a similar period of time. The value of such a study is suggested by the results since in the first series the incidence of evisceration was 0.75 per cent and in the second series 0.60 per cent. More significant perhaps is the difference in mortality rate as that in the first series was 45.45 per cent while in the second series it was 19.04 per cent, a mortality rate of 30.2 per cent for the total of 43 eviscerations.

In the continuation of the comprehensive study of this problem of wound disruption on the surgical service of the New York Hospital, the records of all patients upon whom abdominal operations were performed between September 1, 1932, and January 1, 1940, were reviewed with respect to the following factors: location of the incision, suture material used in closing, the operation performed, the lesion, whether malignant or nonmalignant, and whether infection was present previous to operation or presumably introduced during the operative procedure. Our total of 6,417 abdominal wounds were followed by 43 eviscerations, an incidence of 0.66 per cent. The general information concerning the series is presented in Table I.

In Table II the influence upon the incidence of evisceration of the site of incision and the type of suture material employed, together with an evaluation of the incidence of wound evisceration for the entire period, are presented.

From the Department of Surgery, of the New York Hospital and Cornell University Medical College

Table III approaches the subject from a different viewpoint. Here the figures are given for incidence of evisceration in various operations and again reference is made to the suture material employed.

Table IV summarizes the distribution of suture material employed. It is to be observed that catgut has been used with increasing frequency and we feel that an interpretation of this point is worthy of discussion. The indications for the use of silk have been more rigidly adhered to from year to year. Catgut has, therefore, had to bear the brunt of all cases of infection or possible infection. The incidence of wound evisceration, however, has been almost equal in the two obviating, therefore, any preference for safety in so far as wound closure is concerned.

### TYPES OF CLOSURE

1 *Catgut closure* a Interrupted catgut closure. The peritoneum is closed with a continuous suture of No. 0 plain or No. 1 20 day chromic catgut. The fascia is approximated by a series of interrupted sutures of chromic catgut. No. 1 Stay sutures of silk worm or "dermo" are placed so that they embrace the fascia only.

b Interrupted catgut closure with figure-of-8 sutures. This is a modification of a, instead of interrupted chromic sutures, the figure-of-8 type of suture with No. 1 20 day chromic is employed.

c Interrupted catgut closure with drainage. No. 1 20 day chromic catgut is used to close the peritoneum. Instead of one continuous suture, one continuous suture starts from each extremity of the wound and is brought to the point where the drain emerges. At this point on either side of the drain, a single reinforcing suture of the same material is placed. The single suture is referred to as a "safety suture." The fascia is closed in the manner described and stay sutures complete the closure.

2 *Silk closure* a Silk closure without drainage. A continuous suture of twisted surgical silk No. 7 approximates the peritoneum, and interrupted sutures of the same material unite the fascia. When stay sutures are employed they are of the same silk and form a lateral figure-of-8, in-

TABLE I.—GENERAL INFORMATION

|                                |       |
|--------------------------------|-------|
| Number of abdominal operations | 6,417 |
| Total eviscerations            | 43    |
| Incidence, per cent            | 66    |
| Deaths                         | 4     |
| Mortality per cent             | 30    |

cluding the fascia. The subcutaneous tissues and skin are closed with interrupted silk (No. 5) sutures.

b. Silk closure with drainage. This closure is the same as b in previous list except that silk, No. 7 is used in place of catgut. The safety sutures of silk are employed. Stay sutures may or may not be used; the subcutaneous tissues are not approximated, unless they are unusually thick. Ordinarily the deep skin sutures (No. 5 silk) suffice to bring these tissues into approximation and reaction around the drain is less likely to persist in the surrounding tissues if sutures are omitted.

3. *Silk and catgut closure.* A continuous suture of No. 0 or No. 1 plain catgut or No. 0 or No. 1 chromic catgut is used for the peritoneum. The fascia is approximated by interrupted sutures of twisted surgical silk, No. 7 or figure-of-8 sutures of the same material. Interrupted sutures of silk No. 5 are used to approximate the subcutaneous tissue and skin. Stay sutures, when employed, are buried, consist of double silk, No. 7 and form a vertical figure-of-8 without including muscle.

4. *Silver wire closure.* This is the through-and-through silver wire closure as described by Read, Zinninger and Merrill. A suture of silver wire on an atraumatic needle is introduced from the skin through the subcutaneous tissues and fascia down to and through the peritoneum, and is then returned to the skin, layer by layer. Silver wire sutures of No. 20 round wire should be inserted about 3 centimeters apart and when all have been placed they are drawn taught and each one is secured separately by twisting. No guards to protect the skin from the wires are employed.

In our previous report we warned against the use of silk and catgut in the same wound. The 77 cases reported here of closure of abdominal wounds with silk and catgut show none of the unfavorable complications that we have suggested. The definition of a silk and catgut wound is, however, demanding of explanation. The use of a silk suture, or a catgut suture to the peritoneum with silk ligatures and silk sutures to the fascia, subcutaneous tissue and the skin does not present the same situation as does the use of both catgut and silk material for suture and ligature in the more superficial layers. The use of a long, continuous silk suture to the peritoneum is ob-

TABLE II.—SITE OF INCISION AND SUTURE MATERIAL

| Incision             | Cat gut | Silk | Cat gut and silk | Silver wire | Total | Wound closures | Per cent |
|----------------------|---------|------|------------------|-------------|-------|----------------|----------|
| Upper right rectus   | 543     | 279  | 26               | 829         | 3     | 26             | 12       |
| Upper left rectus    | 26      | 95   |                  | 34          | 19    |                |          |
| Lower right rectus   | 262     | 149  |                  | 26          | 294   |                | 39       |
| Lower left rectus    | 267     | 43   |                  | 30          | 281   |                |          |
| McBurney             | 36      | 1009 | 20               |             | 1077  |                | 28       |
| Upper midline        |         | 15   |                  |             |       |                |          |
| Lower midline        | 105     | 20   |                  | 7           | 14    |                |          |
| Mid midline          |         | 15   |                  |             | 39    |                |          |
| Mid right rectus     | 13      | 60   | 1                | 20          | 34    |                | 30       |
| Mid left rectus      |         |      |                  | 6           |       |                | 54       |
| Transcostal          | 27      |      |                  |             |       |                |          |
| Transverse rectus    |         | 10   |                  |             | 19    |                | 26       |
| Transverse umbilical |         | 60   |                  |             | 66    |                |          |
| Total                | 2070    | 1945 | 77               | 102         | 2417  | 43             | 67       |

jected to by some surgeons because, they contend it produces a permanent distortion of the peritoneum. Furthermore, they object to its use on the ground that if the wound becomes infected a protracted time is required for the expulsion of the continuous silk suture during which period a foreign body stays peristalsis.

We have felt an added security in the use of through-and-through silver wire closures and although the incidence of wound disruption in our series of 385 is 1.30 per cent, we believe that this would have been much higher in the same group of cases with any other suture material. The indications previously set up have been the basis for its use. We recommend that silver wire closure be used in the presence of massive abdominal infection, in wounds which have been grossly contaminated by gastrointestinal contents, and in all cases debilitated by malignancy or long standing chronic disease associated with anemia as well as for the secondary closure of disrupted wounds.

Our experience as detailed in Table V continues to be rather unique in the preponderance of disruption in male patients as compared with other reports in the literature. This is most nearly approached by Meleny and Howes who report 70 per cent eviscerations occurring in male patients. The total incidence here is approximately 20 per cent male patients who have had wound disruptions.

TABLE III—OPERATION, SUTURE MATERIAL

| Operation                | Cat gut | Silk  | Cat gut and silk | Silver wire | Total | Eviscerations | Per cent |
|--------------------------|---------|-------|------------------|-------------|-------|---------------|----------|
| Appendectomy             | 1778    | 1043  | 22               | 8           | 2851  | 5             | 0.17     |
| Biliary tract operations | 1009    | 147   | 32               | 102         | 1290  | 12            | 0.92     |
| Stomach operations       | 383     | 113   | 13               | 136         | 645   | 10            | 1.55     |
| Small bowel operations   | 75      | 28    | 1                | 27          | 131   | 1             | 0.76     |
| Large bowel operations   | 337     | 150   | 3                | 60          | 550   | 11            | 1.96     |
| Pelvic operations        | 178     | 40    | 0                | 2           | 220   | 0             | 0        |
| Exploratory operations   | 132     | 125   | 5                | 27          | 289   | 2             | 0.69     |
| Ventral hernia repair    | 31      | 232   | 0                | 3           | 266   | 2             | 0.75     |
| Splenectomy              | 8       | 52    | 0                | 3           | 63    | 0             | 0        |
| Umbilical hernia repair  | 0       | 12    | 0                | 0           | 12    | 0             | 0        |
| Miscellaneous            | 39      | 34    | 1                | 17          | 91    | 0             | 0        |
| Total                    | 3 970   | 1 985 | 77               | 385         | 6 417 | 43            | 0.65     |

## ANALYSIS OF EVISCERATIONS

No age is immune, evidently, from wound disruption as our youngest patient was 8 months old and the eldest 76 years of age. The majority, however, are to be found in the fifth and sixth decades, or in the age in which malignancy is most likely to occur.

In our previous report we noted that our findings were in agreement with those of many authors in that we reported an incidence of wound disruption of 1.20 per cent in abdominal wounds for malignant disease which was almost twice the incidence of wound disruption in nonmalignant cases. Since that report our experience has been even more striking for in 557 patients with malignant disease there were 10 eviscerations, an incidence of 1.8 per cent. In 1,139 patients with malignant disease there were 16 eviscerations, an incidence of 1.39 per cent, while in the same period 27 eviscerations occurred in 5,278 patients without malignant disease, an incidence of 0.51 per cent, giving us now an incidence of wound disruptions almost 3 times greater in malignant disease than in nonmalignant disease. Paralleling the importance of malignancy from the standpoint of the possibility of wound disruption is the associated high mortality rate, for in the 16 patients having wound disruptions in malignant disease the mortality rate was 56 per cent, whereas in nonmalignant cases the mortality rate was 18.51 per cent.

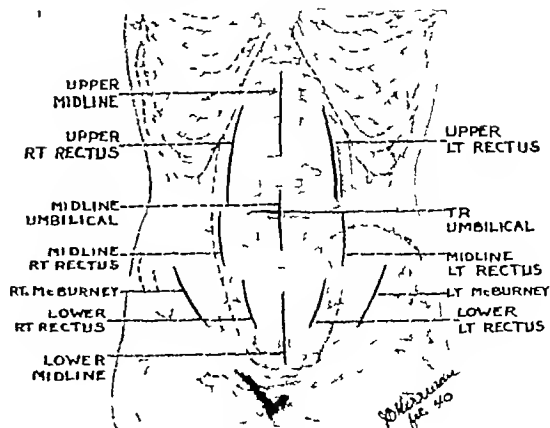


Fig. 1 Location and designation of incisions employed

Of all the known predisposing factors to wound evisceration, debility has received the greatest emphasis. This term is a comprehensive one and is generally used to denote weight loss, weakness, anemia, and early fatigue on exertion, commonly seen in patients suffering from malignant disease and especially those whose malignant lesion is ulcerated with resultant bleeding and infection. In our first series of eviscerations there were 11 patients labeled as being debilitated prior to operation, while in this series of 21 patients there were 8. The red cell count ranged from 2.5 to 5.9 million and in many instances the recorded pre-operative red blood count was done after numerous transfusion. The significance of avitaminosis has become more important in our experience and for this reason we are at the present time insistent that those vitamins known to be concerned with wound healing, in particular

TABLE IV—SUTURE MATERIAL, SUMMARY

| Suture material | Total | Eviscerations | Per cent |
|-----------------|-------|---------------|----------|
| Catgut          | 3 970 | 26            | 0.65     |
| Silk            | 1 985 | 12            | 0.60     |
| Silk and catgut | 77    | 0             | 0        |
| Silver wire     | 385   | 5             | 1.29     |
| Total           | 6,417 | 43            | 0.66     |

TABLE V—EVISCERATION IN MALIGNANCY

|  | Malignant disease | Nonmalignant disease |
|--|-------------------|----------------------|
| Total cases                            | 1,139             | 5,278                |
| Eviscerations                          | 16                | 27                   |
| Incidence, per cent                    | 1.39              | .51                  |
| Mortality from eviscerations, per cent | 56                | 18.51                |



TABLE VI—Continued

| No.<br>Sex<br>Age | Diagnosis               | RBC | HGB | WBC    | Debility | Jaundice | Blood<br>pressure | Arterio-<br>sclerosis | Syphilis | Diabetes | Operation              | Incision | Suture<br>material | Cigarette<br>drains | P.O.<br>days | Contributing factors  | Second<br>ary<br>closure | Discharged<br>P.O.<br>days | Died<br>P.O.<br>day | Follow up | Hernia               |
|-------------------|-------------------------|-----|-----|--------|----------|----------|-------------------|-----------------------|----------|----------|------------------------|----------|--------------------|---------------------|--------------|---|--------------------------|----------------------------|---------------------|-----------|----------------------|
| 61693<br>M<br>58  | Carcinoma of<br>stomach | 4.9 | 102 | 9,850  | 0        | 0        | 160/100           | +                     | 0        | 0        | Exploration<br>biopsy  | U R R    | Silk               | 0                   | 11           | 1 Vomiting<br>2 Distention                                      | Sw                       | 63                         | No<br>autopsy       |           |                      |
| 173219<br>M<br>54 | Carcinoma of<br>stomach | 4.9 | 88  | 6,200  | +        | 0        | 160/96            | +                     | 0        | 0        | Gastric<br>resection   | U R R    | Cg                 | 0                   | 16           | 1 Intestinal obstruction<br>2 kink in distal loop<br>of jejunum | Sw                       | 26                         | 2 yrs<br>later      |           | None                 |
| 226505<br>M<br>64 | Carcinoma of<br>colon   | 4.8 | 96  | 6,100  | 0        | 0        | 210/110           | +                     | 0        | 0        | Resection              | L L R    | Cg                 | 0                   | 10           | 1 Cough<br>2 Distention<br>3 Bronchopneumonia                   | Sw                       | 42                         | 11 mos<br>later     |           | Incisional<br>hernia |
| 132023<br>M<br>59 | Carcinoma of<br>bowel   | 3.9 | 60  | 11,000 | +        | 0        | 120/88            | +                     | 0        | 0        | Ileocecal<br>molestomy | U L R    | Cg                 | 0                   | 8            | 1 Hiccoughs<br>2 Distention<br>3 Peritonitis                    | Silk<br>Wg               | 22                         | Died 6<br>mos later |           |                      |
| 241545<br>M<br>57 | Carcinoma of<br>rectum  | 2.9 | 56  | 4,800  | +        | 0        | 140/85            | +                     | 0        | 0        | Colostomy              | L L R    | Cg                 | 0                   | 5            | 1 Peritonitis<br>2 Vomiting<br>3 Infection                      | Sw                       | 29                         | 6 mos<br>later      |           | None                 |
| 137742<br>M<br>54 | Carcinoma of<br>rectum  | 5   | 92  | 7,200  | +        | 0        | 110/60            | 0                     | 0        | 0        | Exploration            | L L R    | Silk               | 0                   | 5            | 1 Extensive metastases<br>2 Distention<br>3 Bronchopneumonia    | Sw                       |                            | Autopsy             |           |                      |

vitamins B and C, be administered before and after operation parenterally if they cannot be given by mouth

Arteriosclerosis and hypertension, insofar as we have been able to observe, do not play any significant rôle in wound disruption. Diabetes associated with arteriosclerosis and commonly recognized as a factor in lowering resistance to infection has not accounted for a single instance of evisceration in our series. Syphilis, long emphasized in the surgical literature as being responsible for poor healing of wounds, seems to have played no part in our group. Only 2 of these patients were found to have positive Wassermann reactions.

As to their location, the 43 wound disruptions were distributed as follows: Upper right rectus, 26, lower left rectus, 6, upper left rectus, 3, lower right rectus, 3, McBurney, 2, middle right rectus, middle left rectus, and transverse umbilical each one. The upper right rectus incision is by far the one most frequently employed, aside from the McBurney, in operations upon the abdomen. Likewise, it is through this type of incision that operations on the biliary tract have been done. Upper abdominal incisions, it would seem, are more likely to be subjected to greater mechanical strain than those of the lower abdomen. In addition, there is greater likelihood of peritonitis originating in the upper abdomen to spread to the entire peritoneal cavity than when it arises in the lower quadrants where there is a tendency to localize in the pelvis. It is for this reason that gynecological surgery is associated with a low incidence of wound evisceration.

Drains were used in 15 of the 43 patients. It is our general impression that drainage of a wound properly closed does not materially increase the probability of its disruption.

The time of disruption following operation is of significance. Although most disruptions occur between the fifth and tenth day after operation, we have had them occur as early as the first and as late as the thirtieth day. The immediate factors of wound disruption continue to be those associated with upper respiratory infection and abdominal distention. Coughing and vomiting remain the two most common symptoms that appear on the charts of these patients at the time of disruption. It seems unnecessary to stress the importance of combating postoperative pulmonary complications by rebreathing with carbon dioxide, shifting position immediately after operation and doing everything possible to prevent postoperative atelectasis. Persistent vomiting may be controlled by the use of the Wangensteen

method of decompression or Miller Abbott double lumen tube, and we recommend their use for it is believed that this has been of importance in reducing the incidence of wound evisceration.

In these 43 patients, secondary closures were accomplished as follows: 33 with silver wire, 7 with packing and adhesive strapping, 1 with silk, 1 with catgut, and 1 with silkwormgut. Packing and adhesive strapping were used on those patients who were considered too ill even to subject to a secondary closure with silver wire. One of those died and 3 later developed incisional hernias. Following the secondary closure the patients remained in the hospital from 1 to 16 days.

The mortality rate for our entire series of 43 cases is 30.2 per cent. In our first report there were 10 deaths occurring in 2 instances of wound disruption or a mortality rate of 45.45 per cent. In our last 2 disruptions there have been 4 deaths, or a mortality rate of 9.4 per cent. The lowered mortality we attribute to early recognition of the evisceration and to the prompt secondary closure of the wound before dehiscence has taken place through its entire extent.

#### POINTS TO EMPHASIZE

During the past 2 years there has appeared in the surgical literature number of articles favoring the use of silk suture material. Whipple, Jenkins, Shambaugh, Howes, and others have reported their favorable experiences with the use of this suture material. The master of silk surgery<sup>7</sup> was Halsted and it was chiefly his accurate understanding of wound healing and his execution of a meticulous surgical technique that established its use. It may seem logical to assume that an absorbable suture material which will disappear following the healing of the wound would be preferable to one that remains in the tissues, but in clean wounds the amount of reaction about the silk sutures is minimal. It is our opinion that many of the advantages of silk

suture material are based upon the meticulous type of surgery it requires rather than on the strength of the suture material. The terms silk surgeon and catgut surgeon have come to have a definite meaning to the profession. In both groups excellent results have been obtained in the suturing of an abdominal wound. It is therefore important in the consideration of this subject to look upon the problem in a broader sense than the literature indicates at present. We should keep in mind the general status of the patient, his nutrition, whether or not he is anemic, and the disease that has necessitated an operation as well as the structure of the parts involved in the closure of the abdominal wound. The meticulous care exercised by the surgeon in doing an operation should be paralleled by the post-operative care of that individual in order that the anatomical and physiological integrity of the abdominal wall may be re-established in as short a time as possible. When all of these factors are recognized and receive proper attention the incidence of abdominal wound disruption will be further diminished.

#### BIBLIOGRAPHY

- GLUCK, F. and MORSE, S. W. The disruption of abdominal wounds. *Surg. Gynec. & Obst.* 937 65-67.
- HOWES, E. L. A remembrance of suture technique needed. *Am. J. Surg.* 1940, 48 348-352.
- J. VIERA, HENRICH P. A clinical study of catgut in relation to abdominal wound disruption. *Surg. Gynec. & Obst.* 1937 64 648-662.
- MILNER, F. L. and HOWES, E. L. The disruption of abdominal wounds. I. the protrusion of viscera. *Ann. Surg.* 1934, 99, 7-13.
- REID, M. ZORNIGER, M., and MINNELL, P. Closure of the abdomen with through-and-through silver wire sutures in cases of abdominal emergencies. *Ann. Surg.* 1933, 98 890-896.
- SAMMARCO, P. Postoperatively wound complications: clinical study in reference to silk. *Surg. Gynec. & Obst.* 1937 64 795.
- WHIPPLE, A. O. The essential principles in clean wound healing. *Surg. Gynec. & Obst.* 1940, 70 57-60.

# FRACTURES OF THE MANDIBLE

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A COMBINATION of reasons has produced greater interest in fractures of the mandible. The number of such fractures has increased since the advent of the automobile. Today thorough roentgenographic examination reveals many fractures that formerly went unrecognized. Recently devised appliances have made available simple and practical methods of treatment which give encouragement to the novice. The general surgeon has begun to recognize that he has not done his best for the patient if he has not restored normal occlusion.

The many recent papers on fractures of the facial bones and their management disclose a striking lack of agreement in this field of surgery. The missionary work of Kazanjian has done much to bring order out of chaos. He has demonstrated the impracticability of expensive appliances which take days to construct. He has emphasized the importance of training the oral surgeon in the use of mechanical devices. He has overthrown old accepted theories by proving them wrong, to wit, direct wiring and absolute fixation. Many of the principles described herein are either his teachings or slight modifications of them.

The threat of war and the mobilization of medical units has brought before us the need for uniformity of treatment. It is obvious that many of the principles developed by Kazanjian<sup>1</sup> in the last war have not become popular. In civilian hospitals, for instance, we still see complete fixation of one jaw against the other, the use of complicated splints, the covering of wire ends with compound and wax and many other practices which are relics of the past. It is the purpose of this paper to outline the simplest forms of treatment which may be applied to either simple or complicated fractures of the mandible.

**Anatomy** If the thickened portions at the ends of a horseshoe were longer we would have a rough model of the mandible. If these ends were hung between two slings, the outer band of each sling would represent the masseter, and the inner, the internal pterygoid. Between them they support

the ramus of the mandible and act to pull the lower against the upper jaw. These two muscles are like a pair of horses attached to the wagon whipple-tree. The temporal muscles likewise pull the mandible upward. The external pterygoid acts to protrude the lower jaw.

If we combine the action of these muscles, the pull on the shorter fragment, when the fracture is at the angle, is an arc upward and forward (Fig 1). The depressors of the jaw are attached to the anterior portions of the body. Thus we see that the posterior fragment is always pulled upward and forward, the anterior fragment downward and backward.

**Directional plane of fracture** It is also of importance whether the line of fracture is from above to below, backward or forward. If in a unilateral fracture the plane of cleavage is forward, by its very nature the posterior fragment will support the larger anterior one (Fig 2). If on the other hand, the direction is backward there is nothing to prevent the shorter fragment from being dragged upward until the mandible strikes some portion of the upper jaw (Fig 3). Many other elements occur, such as the irregularity of the line of fracture and the position of projecting spurs, teeth in the line of fracture, or, occluding teeth. These all make the problem more complicated.

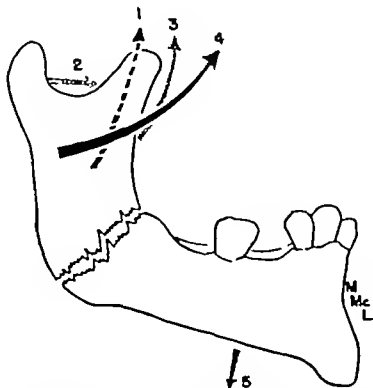


Fig 1 Direction of muscle pull. Arrow 1, direction of pull of the masseter and internal pterygoid. Arrow 2, direction of pull of external pterygoid. Arrow 3, direction of pull of the temporal muscle. Arrow 4, direction of combined pull of all three. Arrow 5, direction of combined pull of the infrahyoid and suprahyoid groups and the digastric and the platysma.

<sup>1</sup>Kazanjian V H Urgent treatment of face and jaw injuries J Am Dental Ass 1926 13 71.

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Fig. 4. The posterior fragment is being pulled in an arc upward but its direction of plane supports the anterior segment.

For many years we have stressed two principles in the care of fractures of the mandible: simplicity in plan of immobilization and prompt reduction. The importance of these basic facts will be shown later. Recent papers tend to lose sight of the fact that complicated splinting causes a loss of time in reduction of the fracture which is often detrimental to the patient. They also involve a costly splint not readily available to clinic patients. The surgeon unfamiliar with the mechanism of such splints is often at a loss to apply them and disturbances of occlusion are frequently the end result.

**Early reduction.** One of the most important lessons which we have learned is the importance of prompt reduction and the necessity for early immobilization. It is for this reason that we illustrate (Fig. 4) a method of application of simple bandage and adhesive with elastic traction which effectively holds the mandible immobilized. This simple method, devised by Karanjanian, is in keeping with the principle that, to be effective treatment must be simple and applicable with the smallest number of special materials and instruments.

**Intermaxillary wiring.** The simplest form of fixation is intermaxillary wiring. A button serves as a hook to which intermaxillary elastics are applied. By gradual traction elastic force reduces a fracture to proper alignment and holds the segments in position. Very few special instruments are required to wire a fractured mandible. We use a 3 gauge annealed brass wire. However many people prefer a finer gauge. For lighter gauge we use stainless steel. Thick blunt needleholders are very useful for applying the button. A pair of wire cutters such as are used by electricians are useful and also a small pair of scissors used by dentists known as crown and bridge scissors.

These buttons differ from the ordinary hook in that there are no free ends to scratch the cheeks or lips. They require no covering of wax or com-



Fig. 5. The posterior fragment will be pulled upward and less unsupported the anterior segment.

pound. They are sufficiently stable to withstand any amount of elastic pull without buckling. They are so shaped as to retain the elastic band without its slipping off. The strands are so uniformly twisted that there is very little danger of the wire breaking even if it becomes necessary to tighten the button at a later visit.

Intermaxillary elastics have been used for many years in orthodontia. In the latter part of the 19th century there was a bitter controversy as to the originator of the intermaxillary elastic as a corrective measure for malocclusion. There is still some debate as to whether Case or the elder Baker first described the method. The use of these elastics in the treatment of fractures of the mandible however owe their popularity to Karanjanian who, returning from the First World War used and taught their use as early as 1910. A recent description in the literature adds little to what has long been known concerning the use of intermaxillary elastics. It leads one to believe that the method therein described is a new method. This is incorrect, inasmuch as the principle is old, and the method has been used by many of us for two decades more or less.

**Method of applying button.** Figures 5 and 6 show the method of applying the intermaxillary button, with the use of a four strand brass wire, 23 gauge. The wire is passed through the interdental embrasure from the buccal to the lingual surface on the tooth and then is passed back to form a loop about a tooth which has been selected because of its strategic location and suitable shape. A second loop is likewise passed about an adjoining tooth. The wire is grasped only at its end since the scratch of the hemostat weakens it sufficiently so that breakage is liable to occur. A needleholder of the short variety grasps each of the four strands. The wire is grasped parallel to its long axis and then by traction the length of the four strands



Fig. 4. Method of application of simple bandage and adhesive with elastic traction which effectively holds the mandible immobilized

equalized. Grasping the four needleholders together and applying traction while the assistant supports the broken bone the needleholders are twisted simultaneously while traction is applied. It is customary to twist the wires always in the one direction, i.e., clockwise, so that should further adjustment by another operator be necessary, he may assume that the wires have been systematically twisted. While the wires are twisted that portion of wire which envelops the tooth is adjusted so that it lies at the cemento-enamel junction where there is a small depression.

As soon as the strand or rope begins to buckle under the twisting motion, the twisting ceases. The twisted strand is then cut one inch from the beginning of the twisted portion, the four ply strand is then grasped with one needleholder. With a circular sweeping motion the rope is then wrapped around to form a complete loop and then is wrapped a second time, the second loop being placed under the first thus burying the free end and preventing it from scraping the soft tissues

of the cheek or lip and from cutting the elastics. The completed button is easily accessible and readily kept clean. It is firm and unyielding, its stability and ease of application makes the standardization of its application worth-while. For ordinary fractures two pairs of such buttons placed opposite each other in each premolar region, are sufficient to keep the mandible immobilized when the buttons are held together by elastics.

However, when in order to secure proper alignment it is necessary to produce traction in one direction or another and the teeth are present, this is easily accomplished by the addition of one or more buttons. In such event the button may be used as an attachment for elastics and as a guy pulley over which the elastic rides to produce force in the desired direction.

The use of elastic force presumes some experience in the practice of orthodontia. Considerable harm may result if teeth are used which are unopposed by antagonistic teeth for, although



Fig. 5



Fig. 6



Fig. 7



Fig. 8



Fig. 9



Fig. 10



Fig. 11



Fig. 12

Fig. 5. The first step is intermaxillary wiring. The first loop is passed beneath the contact points of the teeth.

Fig. 6. The second loop—the wire is guided with

curved hemostat through the space between the teeth back to the buccal surface.

Fig. 7. Forming the bottom—each wire is grasped separately and their lengths equalized. The instruments are pulled firmly as the assistant stretches the jaw. Testing them all clockwise simultaneously and applying traction, gives firm, evenly ripped strand.

Fig. 8. An instrument guides the loop on the lingual to the cemento-enamel junction. Traction ceases when the wire begins to buckle. The wire is cut one inch from the start of the strand.

Fig. 9. It is grasped again parallel to the long axis and without traction swept around in clockwise circular motion.

Fig. 10. Completion of bottom—the end is buried under the bottom, giving it support and preventing trauma.

Fig. 11. Note the stability and ease of access of the bottom which is readily kept clean.

Fig. 12. The bottoms are shown connected with short elastic band.

this traction is gentle, it is continuous and such a force is tremendous enough so that teeth can be completely lifted from their sockets in 24 hours. Should such an accident occur the wire and elastics should be promptly removed and rest will encourage the tooth to return to its original position.

In fractures of long standing where considerable deformity exists, 48 hours suffice to draw fragments,

although bound down by fibrous adhesions, to their proper alignment. The one rule without exception is that no tooth or group of teeth without occluding teeth in the opposite jaw should ever be used to support a bottom to which elastic traction is applied.

The most important guide to proper alignment is the occlusion. However there are several misleading factors about the meeting of the teeth of

one jaw with those of the other. The patient may have had an abnormal occlusion before the fracture, in other words he may have had a protruding or a retruding jaw. If there was protrusion of the mandibular teeth we occasionally have attempted to correct such a protrusion if this could be accomplished with benefit to the masticatory apparatus.

It sometimes occurs that after considerable effort in attempting proper reduction some space still exists between the anterior teeth. It must be remembered that pipe smokers wear teeth down so that there is often a space for the pipestem. This can be misleading.

The buttons are connected with a short elastic band which may be seen in Figure 12. In event that no elastics such as are used in orthodontia are available one may make his own short elastics. A knot may be tied in a long elastic, or bands may be cut from rubber tubing. The band need not be wrapped more than twice.

It is not necessary to fix the jaws so that it is impossible for the mouth to be opened. On the contrary, it is only necessary to hold the jaw in occlusion without force. The sudden forceful opening, as in yawning or sneezing, does no harm. We believe with Kazanjian that the ability of the patient occasionally to open the mouth a little stimulates healing. Intermaxillary elastics have other advantages. They are readily replaced without affecting the wiring or causing pain, thus permitting frequent examination of the mouth. This allows one to remove the wiring at the earliest possible moment, thus eliminating the old standard term of fixation for long periods. It also allows frequent and thorough cleaning of the oral cavity. In case a general anesthetic has to be administered, elastics need not be applied until after the patient has recovered sufficiently so as to preclude the risk of postoperative nausea. If there has been great displacement and immediate immobilization has been delayed because

of complications, as in the presence of head injuries, the elastic will by its constant though gentle force reduce without trauma the fragments to proper alignment. In epileptics, who frequently fracture the mandible, the elastics are so quickly removed as to be of great value. Further, in those cases in which the wiring needs to be modified from time to time the elastic simplifies matters a great deal.

#### CONCLUSION

Responsibility attending the care of fractures of the mandible has increased. No longer can the general surgeon be content with union regardless of resulting occlusion, no longer can the dentist be satisfied with union regardless of the number of teeth sacrificed, no longer can the oral surgeon be content to wire the mandible for long periods of time while his patient goes on losing weight and feeling like a muzzled dog.

Properly immobilized fractures of the mandible need not be fixed for the long periods that the textbook prescribes. We have many cases which have been immobilized for less than 15 days.

The intermaxillary elastic presents a method of immobilization which is simple and inexpensive and easily applied. It has the advantage of allowing frequent inspection and cleaning of the teeth. It may be readily applied, if a general anesthetic has been given, after the patient awakens, thus avoiding the danger of nausea. It permits enough physiological movement to encourage healing. It prevents trauma to the teeth as in sudden yawning. It permits in the latter days of fixation the ingestion of semi-solid foods. While ingenuity in the application of the various devices at the disposal of the attending general or oral surgeon is not only desirable but necessary, still the practitioner who sees only occasional fractures of the mandible would do well to acquaint himself with certain standard forms of treatment for the usual forms of fractures of the mandible.

# PREVENTION OF WOUND DISRUPTION WITH THROUGH AND THROUGH SILVER WIRE STAY SUTURES

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THE failure of abdominal wounds to heal properly and the resulting complications—wound disruption, infection, and post-operative hernia—still remain a serious problem. Most recent articles on the subject are concerned primarily with the various factors influencing wound healing, such as location of the incision, the suture material used, type of operation, dietary deficiency, imbalance of blood constituents, and the presence of jaundice, malignancy, or infection, rather than with the method of closure of the wound.

We wish to describe a method of closure that has proved entirely satisfactory in preventing disruption of wounds. It consists in the use of through-and-through silver wire sutures in addition to complete closure of the wound in layers.

The patients included in this report were operated upon and followed during the past 8 years at the New York Hospital, and in all, major operative procedures were performed with the use of longitudinal rectus incisions. This study would seem to indicate that the most important single factor in evisceration is the type of closure, since separation of the wound has been avoided by the use of the closure to be described.

Needless to say its efficiency in relation to postoperative infection and hernia depends in large part upon the strict observance of the cardinal principles of surgery: asepsis, complete hemostasis, and gentle handling of tissues. For full discussion of additional factors influencing wound healing, other papers may be consulted (1, 6, 7, 8, 11, 13, 16, 7).

During the past 10 years several reports (3, 3, 4, 9) have given adequate statistical reviews on the subject of evisceration from the point of view of suture material, type of operation, and location of incision. These observers have found the incidence of wound disruption to range from 1 to 3 per cent, with a mortality varying from 18 to 50 per cent, in spite of the various types of wound closure. However, Kennedy (10) in 1928 reported very satisfactory results with

through-and-through closure in which all worm gut was used. Likewise, Rekl, Zimlinger and Merrell (14) in 1933, reported a method of abdominal closure with through-and-through silver wire and demonstrated that this closure was of particular value in patients who had serious intra-abdominal traumatic injuries. In their hands there was no instance of evisceration in the 334 cases operated upon. However, there are technical objections to this simple through-and-through closure. One is the tendency for the wires to be closed so tightly that, with the development of postoperative edema of the wound, the wires cut into the tissues and the subsequent pressure necrosis causes pain and a high incidence of infection. Second, it is impossible to approximate the various layers accurately and, therefore, the incidence of postoperative hernia is high. In an effort to eliminate these objections a modification in the technique has been introduced, i.e., the closure of the wound in layers, in addition to the use of through-and-through silver wires. Undoubtedly this closure has been used from time to time in various clinics, but it has not received enough emphasis to be accepted as a routine in certain types of patients. This closure should not, of course, be used in all types of cases; rather its use should depend upon the operation and the pathology and the age and condition of the patient. Since through-and-through silver wire with closure in layers requires more time, it cannot entirely replace simple through-and-through closure in those patients in whom rapid closure is necessary. Likewise, the latter is the ideal method for repair of disrupted wounds.

Following is a description of the type of closure advocated. As shown in Figure 1, the silver wires (30 gauge) are inserted straight through all layers of the abdominal wall, including peritoneum, about 1 inch from the skin edge and placed about 3/4 inches apart. An atraumatic needle is used in order that the silver wire can be introduced easily and without injury to the tissue. If such a needle is not available, a large cutting-edge needle similar to that used for inserting tension sutures may be used if the short end of the silver wire is turned back and crushed together where it passes through the eye of the needle. Following the in-

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Wounds in which all layers separated, including peritoneum, with or without evisceration were considered as disrupted wounds.

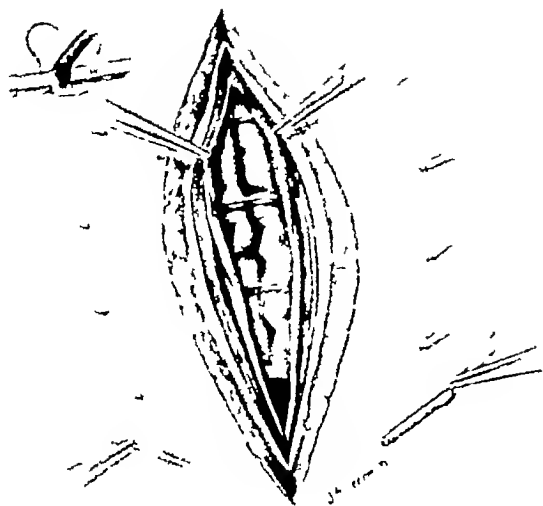


Fig. 1

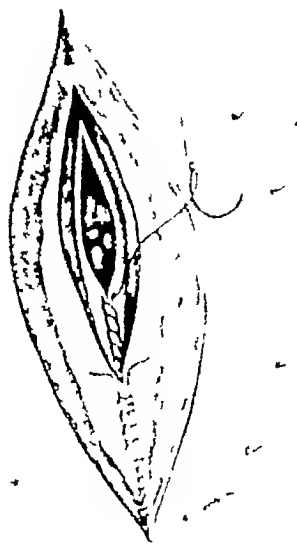


Fig. 2

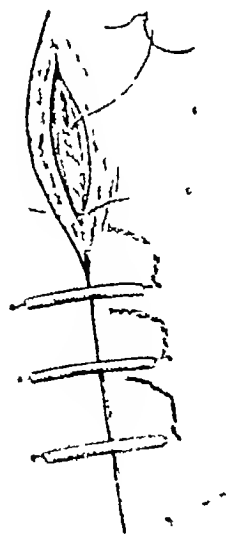


Fig. 3

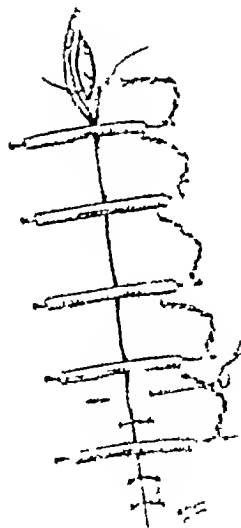


Fig. 4

section of the silver wires, the peritoneum is closed with a continuous suture of catgut for a distance of about one half to three fourths of the wound, and the viscera is approximated for a somewhat smaller distance (Fig. 3).

As shown in Figure 3, the silver wires for that portion of the wound that has already been closed

are then twisted down in place. It is important that the operator place his finger within the abdomen when the wires are being twisted down to prevent omentum or viscera from being caught between the silver wires and the peritoneum and the wires should be twisted 6 to 8 times to prevent their opening. With the exception of the

TABLE I.—TYPE OF CLOSURE

| Type of closure                                      | Total cases | Wound infection |       | Post-operative hernia |      | Wound disruption |     |
|--|-------------|-----------------|-------|-----------------------|------|------------------|-----|
|  |             | No.             | %     | No.                   | %    | No.              | %   |
| Through and through with closure in layers           | 164         |                 |       | 23                    |      |                  |     |
| Simple through and through without closure in layers | 166         | 27              | 16.25 | 16                    | 9.63 |                  | 6.1 |

\*Since this report includes only those patients who were used from those operations and were followed after operation, patients are excluded who died or who were lost to follow-up examinations. (Ginn and Moore (3) have reviewed all operations occurring in New York Hospital). Their percentage of complications for (1) through and through with closure per cent., (2) simple through and through per cent.

upper inch, the remaining part of the wound is then closed in layers, and, with the upper end of the wound still open, the remaining silver wires are twisted down in place. The upper part of the wound must be kept open until all the wires are twisted in place, so that the operator can keep one finger in the abdomen to prevent strangulation of the viscera between the silver wire and the peritoneum. After twisting down all the silver wires, the small remaining portion of the open wound is closed in layers, and the skin is approximated with interrupted fine silk sutures.

The most important feature of this closure is that the silver wires should not be closed too tightly. It should be possible to place one finger easily between the silver wires and the skin after the wires are in place. Small caliber suture material (chromic catgut No. 0 or silk) is preferred for the layer closure so as to reduce the amount of foreign body in the wound. Rubber guards for the silver wire may or may not be used. In the absence of infection, the wires may be removed safely on the fourteenth to sixteenth day where as, in simple through-and-through-closure, the wires should not be removed until the twentieth to twenty first day. After the use of any variety of through-and-through closure the complication of extension of infection from the wound into the peritoneal cavity has never been observed. There has been no wound disruption and, with the exception of silk closure, the incidence of postoperative infection and hernia is considerably less than in any other type of closure, (Table I).

It will be seen from Table II that the cases in which the two methods of closure were used were similar.

In clean cases—exploratory laparotomy cholecystectomy for chronic cholecystitis—in which the laparotomy wound was closed with silk, wound disruption, infection, and postoperative hernia occurred in less than 1 per cent. In a similar group of cases in which the laparotomy wound

TABLE II.—CONDITIONS FOR WHICH OPERATION WAS DONE

|                             | Through and through with closure in layers |    | Simple through and through without closure in layers |   |
|-----------------------------|--|----|--|---|
|                             | No.  | %  | No.  | % |
| Perforated peptic ulcer     |  |    |  |   |
| Gastric resection           | 10   | 30 |  |   |
| Secondary gastric resection |  |    |  |   |
| Posterior gastro-entostomy  | 6  |    |  |   |
| Cyclocholecystomy           | 12   |    |  |   |
| Cholecystectomy             | 18   | 55 |  |   |
| Site of resection           | 16   | 16 | 5  |   |
| Exploratory laparotomy      |  |    |  |   |
| Miscellaneous               | 164  |    | 16   |   |

was closed with catgut, wound disruption occurred in 2 per cent, infection occurred in 16 per cent, and postoperative hernia in 9 per cent. This comparison emphasizes the advantage of a silk closure of the clean wound when the closure is done by those familiar with silk technique.

#### CONCLUSIONS

It is not advocated that the closure described should replace all other types, particularly silk, but it can be used to great advantage in certain patients.

Its advantages are (1) a secure closure without fear of evisceration, (2) elimination of the objections to simple through-and-through closure, with the results that the patient does not suffer from a painful wound, that the incidence of infection and postoperative hernia is greatly reduced, and that a satisfactory scar is obtained.

It is an ideal closure for (1) all patients on whom the gastro-intestinal tract has been opened, (2) patients in whom there is acute intra-abdominal infection, (3) patients who are old and debilitated whom it might be advantageous to get up at an early postoperative date. (4) patients who for one reason or another may have a delayed wound healing, with the possibility of wound disruption.

#### BIBLIOGRAPHY

1. ARRY, LESLIE B. Wound healing. *Physiol. Rev.* 1956, 6: 377.
2. COLE, RALPH. Disruption of abdominal wounds. *Ann. Surg.* 1954, 99: 14.
3. FALLER, L. S. Postoperatively caused separation, reversal of cases. *Surgery* 1937, 5: 3.
4. GINN, FRA. K. and MOORE, G. W. Disruption abdominal wounds. *Surg. Gynec. & Obst.* 1937, 65: 6.

- 5 Idem Personal communication
- 6 HALSTED, WM S Ligation and suture material J Am M Ass, 1913, 60 110
- 7 HOLMAN, EMILE Vitamin and protein factors in pre operative and postoperative care of the surgical patient Surg, Gynec. & Obst, 1940, 70 261
- 8 HOWES, EDWARD L, and HARVLY, SAMUEL C Tissue response to catgut absorption and wound healing Internat. J Med & Surg, 1930, 43 275
- 9 JENKINS HILGER P A clinical study of catgut in relation to abdominal wound disruption Surg, Gynec & Obst, 1937, 64 648
- 10 KENNEDY, J W Practical Surgery of Joseph Price Hospital Philadelphia I A Davis Co, 1928
- 11 LINDMAN THOMAS H, and INCALLS THEODORE H Vitamin C Deficiency and Wound Healing Ann Surg, 1937, 105 616
- 12 MAES, U BOYCH, I F, and McLETRICK, I M Post operative excision Ann Surg 1934 100 968
- 13 MELENEY, IRANK L The control of wound infections Transactions of the New York Surgical Society Ann Surg, 1933, 98 151
- 14 KLID, MONT R, ZINNINGER, M M, and MERRELL, PAUL Closure of the abdomen with through and through silver wire in cases of acute abdominal emergencies Ann Surg, 1933, 98 890
- 15 SOKOLOV, S Postoperative rupture of abdominal wounds with protrusion or prolapse of the viscera (Die postoperative Ruptur der Bauchwunde mit Hervortreten oder Vorfall der Eingeweide) Vestnik Khir, 1931, 65/66 219, Abstract in Internat Abst Surg, 1932, 55 157
- 16 THOMPSON, W D, RAVEN, I S, and IRANK, IRVING L Effect of hypoproteinemia on wound disruption Arch Surg 1938, 36 500
- 17 WHIPPLE, ALFRED O, and ELLIOTT, ROBT H E, JR The repair of abdominal incisions Ann Surg, 1938, 108 741



# THE USE OF ALLOY STEEL WIRE IN THE CLOSURE OF ABDOMINAL WOUNDS

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SINCE the introduction of alloy steel wire by Babcock (1, 2) this material has been employed with increasing frequency at the Cleveland Clinic for the closure of abdominal wounds. The incidence of abdominal wound morbidity has been reduced to such an extent that we believe a further report of its use would be of interest. A technique of closure with alloy steel wire is presented, and the incidence of wound infection and disruption is contrasted with antecedent methods and materials.

The use of wire sutures in the closure of abdominal wounds is not of recent origin. Historical reviews have been presented by Kraissl in 1936, and by Kaufman, Johnson, and Lesmer in 1939. Following the first reports of Babcock, a number of articles appeared in the literature describing the advantages of alloy steel wire sutures. Dextrin closed the abdomen in two layers, the first including all planes except the skin and subcutaneous tissues which were included in the second. In his experience, the advantages of alloy steel wire were: (1) It was tolerated well by the tissues, (2) it could be used in the presence of infection, and (3) it produced solid closure and emprovements were rare. Complaints of discomfort from wire knots were infrequent. It was occasionally necessary to remove a suture which acted as a nidus for a draining sinus.

Wells closed the peritoneum and posterior fascia with catgut and the anterior fascia with interrupted alloy steel sutures. Jenkins, in reviewing the experience of Babcock, stated that a larger percentage of wounds healed by first intention and that alloy steel was the most satisfactory suture material for use in infected fields because there was no tendency to sinus formation. Kaufman, Johnson, and Lesmer found that the incidence of wound infection in the repair of hernias was markedly reduced when alloy steel wire was used. Preston showed that the tensile strength of wounds sutured with alloy steel wire was greater than that of those closed with silk or catgut. Several cases were reported demonstrating the absence of a tendency to produce draining sinuses in the presence of an infected field.

From the Cleveland Clinic

One of the first clinical impressions of alloy steel wire used alone without stay sutures in the closure of abdominal wounds was the frequency of satisfactory healing, regardless of such adverse factors as carcinomatous, deep jaundice, and general cachexia. Disruption was rare, despite the fact that wire was used in all of the more severe abdominal operations when this accident was feared. Wound infection seemed to be reduced markedly.

In order to confirm or deny this satisfactory clinical appraisal of wire sutured wounds, separate studies were made to compare the incidence of wound disruption and infection with other methods of abdominal closure.

**Wound disruption.** From January 1, 1930, to January 1, 1940, a group of surgeons at the Cleveland Clinic performed 4,554 consecutive laparotomies with 44 disruptions, an incidence of 1.05 per cent. This compares favorably with most of the reports in the literature (3, 8, 9). Fifteen deaths in the 44 cases were attributable to disruption, a mortality rate of 34 per cent. The mortality rate from this accident is quoted in the literature from 8 to 53 per cent (3, 6, 8, 9).

A detailed study of these 44 cases revealed that more than half of the disruptions occurred in upper rectus incisions, and that the highest incidence was found in operations on the biliary tract. This is in accordance with the findings in the series reported by McIneny and Howes. The disruptions according to the locations of the incisions were as follows: upper rectus, 23; lower rectus, 7; upper midline, 6; lower midline, 5; other locations, 3; a total of 44.

Although it was difficult to obtain accurate information regarding the predisposing causes, abdominal distention with vomiting occurred to a fairly severe degree in 30 to 40 per cent of the cases. Wound infection and drainage of bile and pancreatic juices was the second major cause, and was found in 30 per cent. Because of the rapid digestion of the catgut, biliary and pancreatic drainage are probably of paramount importance in disruption of wounds closed with catgut, as compared to those closed with nonabsorbable sutures.

In view of the high incidence of disruption in upper rectus incisions, especially in those made for operations on the biliary tract, a consecutive series from January 1, 1937, to January 1, 1940, was selected for a comparative study of wound disruption with various types of closure and suture materials. In this period, 193 operations were performed by members of the surgical staff, with 11 disruptions, an incidence of 5.7 per cent. Of 54 wounds closed in layers with catgut alone, either continuous or interrupted sutures, 6, or 11 per cent, disrupted. In 58 cases the wounds were sutured with continuous catgut sutures to the peritoneum and posterior rectus fascia, and with interrupted alloy steel wire to the anterior rectus fascia. In this group 4, or 6 per cent, of the wounds disrupted. Buried interrupted figure-of-eight alloy steel sutures were used to close 81 wounds. No stay sutures were used. Only one disruption occurred with this type of closure, an incidence of 1.2 per cent (Table I). The fact that nearly all the severe cases with jaundice and malignancy of the head of the pancreas were found in the last group adds significance to the results.

**Wound infection.** The total experience with abdominal wound healing in combined abdominoperineal resections for carcinoma of the rectum done by one surgeon (T. E. J.) was reviewed, and the morbidity in various types of closure of the abdominal wound was compared. This operation was selected for study because of the high incidence of infection in wounds closed with catgut and supporting stay sutures.

In order that a strictly comparable series could be obtained, 256 consecutive cases fulfilling the following requirements were taken from a total series of 366 cases: (1) The operation was a one stage combined abdominoperineal resection, (2) the colostomy was brought out of the abdomen through a midline incision, and (3) the technique of the operation was the same. Two stage resections, inguinal colostomies, preliminary cecosto-

TABLE I — ABDOMINAL WOUND DISRUPTION I OPERATIONS ON THE BILIARY TRACT<sup>1</sup>

| Suture material                                     | No. cases | No. disruptions | Per cent |
|---|-----------|-----------------|----------|
| Catgut (all layers)                                 | 54        | 6               | 11.0     |
| Catgut and alloy steel wire                         | 58        | 4               | 6.9      |
| Alloy steel figure-of-eight sutures no stay sutures | 81        | 1               | 1.2      |

<sup>1</sup>Comparison of Suture Material in 193 Consecutive Cases January 1937, to January 1940

mies, and cases in which death occurred, except those attributable to wound morbidity, were excluded.

This series classified itself, in chronological sequence, into 3 groups. In Group I (76 cases), the abdominal wound was closed in layers with catgut and reinforced with silkworm gut stay sutures. In Group II (64 cases), the peritoneum and posterior rectus fascia were closed with catgut and the anterior rectus sheath, with interrupted alloy steel sutures. Stay sutures were not used. In Group III (116 cases), the abdomen was closed with alloy steel figure-of-eight sutures alone, including all layers except the skin and subcutaneous tissues. Stay sutures were not used. In all of the groups the hemostatic ligature was fine No. 000 chromic catgut. The skin was closed with clips. No sutures were used in the subcutaneous tissues, even in obese patients.

Wound infections were clinically classified as slight, moderate, and severe. A small localized subcutaneous infection was considered slight. Definite abscesses superficial or deep to the anterior rectus fascia, but which healed before the normally expected hospital discharge, were classified as moderate. Infections which seriously endangered the life of the patient or prolonged hospitalization, or those to which death was attributable, were classified as severe.

As shown in Table II, in Group I, 27.5 per cent of the wounds became infected. Disruption occurred in 3 wounds, or 3.9 per cent, once because

TABLE II — ABDOMINAL WOUND MORBIDITY IN ONE STAGE COMBINED ABDOMINOPERINEAL RESECTIONS<sup>1</sup>

| Group | Type of closure                                     | Infections |        |          |        |          | Disruptions |          |
|-------|---|------------|--------|----------|--------|----------|-------------|----------|
|       |   | No. Cases  | Slight | Moderate | Severe | Per cent | No. cases   | Per cent |
| I     | Catgut in layers with stay sutures                  | 76         | 3      | 17       | 3      | 27.5     | 3           | 3.9      |
| II    | Catgut and alloy steel No stay sutures              | 64         | 0      | 7        | 2      | 14.0     | 0           | 0.0      |
| III   | Alloy steel figure-of-eight sutures No stay sutures | 116        | 0      | 1        | 0      | 0.85     | 0           | 0.0      |

<sup>1</sup>A Comparison of Types of Wound Closure in 256 Cases

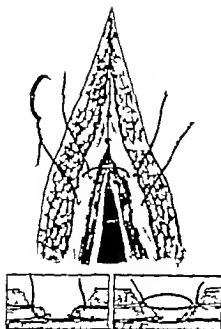


Fig. 2

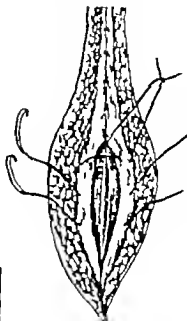


Fig. 3a



Fig. 3b

of infection and twice in the presence of apparent clean healing. Two of these patients died of peritonitis as a result of the disruption. In Group II infection developed in 14 per cent of the wounds. There were no disruptions. In Group III only 1 wound infection occurred, an incidence of 0.85 per cent. This occurred in the seventh case of the group. In the last 100 consecutive one stage abdominoperineal resections for carcinoma of the rectum, with midline colostomies and closed with alloy steel figure-of-eight sutures, there has not been a single infected wound.

No strictly comparable figures on the incidence of hernia in the 3 groups can be quoted, since the follow-up in Group III has not been of sufficient length of time, but we have yet to see a hernia or weakness of the wound about the colostomy where wire figure-of-eight sutures were used.

#### TECHNIQUE

A method of closure of abdominal wounds with alloy steel wire employing Smead's stitch, is shown in the accompanying diagrams. A figure-of-eight suture passes first through anterior fascia, muscle, posterior fascia, and peritoneum (Fig. 1a) and again through the anterior fascia in the

same direction (Fig. 1b). After three-fourths of the wound is closed, the remaining fourth is loaded with the first part of the interrupted stitch (Fig. 2). Each suture is then completed in turn.

The wire ends are cut flush with the jaws of a hemostat which is clamped snugly against the knot (Fig. 3a). The hemostat is then rotated 90 degrees, turning the ends downward (Fig. 3b). A smooth knot is thus presented to the subcutaneous tissues, in which no sutures are placed. The skin is closed with metal clips.

Certain technical details in regard to the type of suture and the handling of the wire itself must be adhered to: (1) The proper amount of tension must be exerted in tying the suture to approximate, but not constrict, the tissues. (2) The knot must be square. (3) The ends of the wire must be turned down carefully. (4) Kinking must be avoided since the wire will break at this point. Wire handles differently from silk or catgut, but, with experience, it may be used with equal facility.

As the figure-of-eight sutures are pulled taut, each plane of the wound is well approximated. No more accurate closure can be accomplished by sutures in layers. Digital palpation of the peritoneum shows a perfectly smooth wound surface.

This stitch was devised by Dr. Louis Smead, of Toledo, Ohio, during his residency in surgery under Dr. John F. Keen at the University of Michigan. It has been advised by personal communication that descriptions of this stitch has not been published to date.

## ADVANTAGES AND DISADVANTAGES

During the past 3½ years, alloy steel wire alone has been chosen with increasing frequency for the closure of abdominal wounds by the members of the surgical staff of the Cleveland Clinic. It is now used extensively in operations on the biliary tract, for benign lesions of the stomach and duodenum, and routinely in operations for gastro-intestinal and other abdominal malignancies in both the upper and lower abdomen.

The routine use in gastro-intestinal malignancies deserves note. The marked decrease in wound complications has been a major factor in the reduction of postoperative morbidity and hospital mortality. The series of combined abdominoperitoneal resections presented typifies the entire experience.

Most clean laparotomy wounds can be closed satisfactorily with catgut, silk, or cotton. However, when actual or potential wound infection exists, or when disruption is feared, we believe that better results can be obtained with steel wire. Steel-closed wounds heal with very little tissue reaction to the suture material. In this respect steel is similar to silk, but it has an added advantage in that the production of chronic draining sinuses is rare, even in the presence of a grossly infected field. The induration and grayish, necrotic foci about catgut is in sharp contrast to the clean, reactionless healing in the presence of wire.

The disadvantages of steel wire are few. Rarely, a suture will perpetuate a draining sinus. It has been necessary to remove sutures for this reason in only 2 instances. Occasionally, a patient with scanty subcutaneous tissue will complain of discomfort about a knot but it is a simple procedure to locate and remove the offending suture under local anesthesia.

We believe that alloy steel wire is indispensable in operations for gastro-intestinal malignancies, and so advantageous in many other procedures that its few disadvantages are greatly outweighed.

## SUMMARY

1. The use of buried alloy steel sutures alone without stay sutures for the closure of abdominal

wounds has reduced wound morbidity to an extremely low incidence.

2. The incidence of wound disruption in operations on the biliary tract has been reduced from 11 per cent in closures with catgut to 1.2 per cent in wounds closed with alloy steel figure-of-eight sutures alone.

3. The incidence of infection in abdominal wounds in combined abdominoperitoneal resections with midline colostomies has been reduced from 27.5 per cent with the use of catgut in layers and stay sutures to 0.85 per cent with the use of interrupted figure-of-eight alloy steel sutures.

4. A method of closing abdominal wounds with wire is presented.

## BIBLIOGRAPHY

1. BABCOCK, W. WAYNE. Ligatures and sutures of alloy steel wire. *J Am M Ass*, 1934, 102: 1756-1757.
2. Idem. Catgut allergy with note on use of alloy steel wire for sutures and ligatures. *Am J Surg*, 1935, 27: 67-70.
3. COLP, R. Disruption of abdominal wounds. *Ann Surg*, 1934, 99: 14-27.
4. DAMBRIN, C. Sutures des parois abdominales à l'aide de fils de fer perdus. *Mém Acad de chir*, 1937, 63: 1269-1272.
5. GENKINS, MORRIS H. The alloy steel wire (Babcock) suture. *Pennsylvania M J*, 1939, 41: 707-709.
6. KAUFMAN, LOUIS RENÉ, JOHNSON, WILLIAM W., and LESSER, ALBERT. Clinical study of alloy steel wire sutures in hernia repair. *Surg, Gynec & Obst*, 1939, 69: 684-687.
7. KRAISSL, CORNELIUS J. Suture material review of recent literature. *Internat. Abstr Surg*, 1936, 62: 417-423.
8. MELENEY, FRANK L., and HOWES, EDWARD L. The disruption of abdominal wounds with the protrusion of viscera. *Ann Surg*, 1934, 99: 5-13.
9. NORRIS, JAMES D. Review of wound healing and mechanics of dehiscence. *Surgery*, 1939, 5: 775-786.
10. PRESTON, DANIEL J. Effect of sutures on strength of healing wounds (with notes on clinical use of alloy steel wire sutures). *Am J Surg*, 1940, 49: 56-63.
11. SMEAD, LOUIS. Personal communication, September, 1940.
12. WELTI, H. Un nouveau matériel de suture non résorbable fil d'acier inoxydable. *Mém Acad de chir*, 1937, 63: 712-714.
13. WHITE, W. C. Disruption of abdominal wounds. *Ann Surg*, 1934, 99: 34-38.

# ACUTE AND CHRONIC INTRA ABDOMINAL LYMPHADENOPATHY

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**L**YMPHADENOPATHIES of one kind or another are well known to the profession in regional areas of the body other than the mesenteric area where their secluded position has served until recently to prevent sufficient examination and study. It appears that the adenopathies of the abdominal field are identical with those of other regions of the body—that the lesion may be acute or chronic and of varying degrees of intensity—that some lymphadenopathies in the mesenteric area are of maximum grade while others, the great majority of the instances, are apparently simple and more benign cases of mesenteric adenitis. It is the last group that we have especially under discussion. In some types the etiology is well known in others it is still under discussion, and to these the term "nonspecific" has been applied.

The term nonspecific as used in this communication is intended to convey the thought that the essential cause of the glandular enlargement under discussion was not specifically known at the present writing or that the adenitis had a potential multiple form of etiology. The term might be better paraphrased as nonclassifiable. Except as an incidental matter unavoidably provoked by the discussion of nonspecific mesenteric adenitis, there will be no reference therefore to specific forms of lymphadenopathy—due either to a specific infecting agent such as those causing typhoid, tuberculous, leptic, or other disease, or to neoplastic change such as the forms of lymphosarcoma, or those bordering upon inflammatory or neoplastic disease such as Hodgkin's disease.

A previous communication summarized all available knowledge concerning the anatomy and physiology of the intra-abdominal lymph nodes, including the usual type of structural arrangement and its "normal variations." The normal functional processes (physiology) and the effects upon the latter of age, nutrition, environment, growth, etc., and of certain abnormal conditions of the body such as fever, anemia, etc., were all gone into exhaustively. It does not seem necessary to repeat this factual knowledge, and those interested sufficiently are referred to the original paper or to the standard works on anatomy and physiology.

It seems important, however, to comment again upon the variable size of the nodes when distinguishing between normal and abnormally enlarged glands and this factor is especially important in the long standing, chronic conditions. It seems that there are as yet no certain measures of the normal variation in size of the mesenteric and other lymph glands and that the lymphatic tissue and glands may be considerably more developed than have hitherto been assumed. In the previous study I pointed out the possibility that in many of the published cases the size of many of the observed intra-abdominal glands may have possibly been within normal limits and that, as a consequence, fundamental errors of diagnosis were possible in reference to any observed symptomatology in such lymph nodes.

A constant variable physiological fluctuation during the different phases of life occurs in the midst of relatively healthy periods. It is a nonspecific phenomenon common to very many diseases. For instance, fever has an effect on the lymph nodes which is characterized by decreasing the delivery phenomena of the lymph nodes into the peripheral circulation. This has recently been studied by Donn. Unless the period of sustained fever is unduly prolonged increased circulation and regeneration occurs fairly quickly and this can be measured in terms of the leucocytosis which follows.

The superlatively developed absorption function of the intestinal tract combined with the constant presence of bacteria in the intestinal lumen creates a situation in which the passage of bacteria from the bowel interior into the associated lymphatic vessels and glands must be considered an almost normal and physiological phenomenon. Although manifestations of the reaction of the host's defense mechanism against this continuous onslaught of bacteria (i.e. disease) are not apparent, it must be true that lymphatic enlargement will take place and in certain instances persist. In the ordinary stress of health and disease and under the proper circumstances, this fact would tend to complicate attempts at integration of the presence of mesenteric nodes into a given syndrome in which other pathology is not demonstrable.

# WILENSKY INTRA-ABDOMINAL LYMPHADENOPATHY

differentiation between acute and chronic is sometimes more or less of an artefact, sometimes the chronic cases are simply those of succession of acute episodes has taken place by intervals in which the symptom is less intense or in which it has subsided even to the point where the symptom is tolerated so completely as to make the believe they have disappeared entirely. In case the chronic anatomical changes clearly characterize the pathological picture probably accounts for the peculiar percentages in Foster's series

## ROENTGENOLOGY

Commonly roentgenographic study of the abdominal viscera—gastro intestinal series, etc.—

no abnormality in the usual normal conditions, roentgen observation shows that the stomach empties continuously and barium passes steadily in normal direction, reaching the cecum in  $1\frac{1}{2}$  to 2 hours. Each successive film shows progress distally the position of the head of the barium column. The segmental peristaltic movements flow smoothly and are promptly followed by normal relaxation of the intestinal wall. If there is delay in movement, the ileum should be seen in 9 hours. The barium mass in the normal intestine is usually continuous, that is, not broken up into separate small oval boluses. The length of normal, barium filled loops varies from 20 to 30 centimeters, and is usually 20 to 25 centimeters.

In association with acute symptoms Golden and Reeves observed the following manifestations of disturbed small intestinal physiology: "(1) localized spasm, i.e., narrowing of a small segment adjacent to the calcified node, either temporary following a peristaltic wave or persistent, (2) persistent generalized spasm of a group of small intestinal loops in the region of the diseased nodes, (3) delay in the passage of barium at the site of the calcified node, (4) delay in the emptying of the ileum for periods of over nine hours." In both the acute and chronic cases calcifications are sometimes visible roentgenographically. In the acute cases the coincidence is usually disregarded. In the chronic cases they are differently considered.

Golden and Reeves point out "the possibility that the roentgenographically observed disturbance of physiology in the intestine may be an explanation for the symptoms often associated with calcified mesenteric lymph nodes. The disturbances in small intestinal physiology include spasm and seemed to take place in loops of intestine

directly adjacent to calcified nodes." A questioning attitude concerning the relationship of roentgenographically demonstrated calcified abdominal lymph nodes and the symptom complex which an individual patient presents is necessary. This questioning attitude is advisable because it is not necessarily so that the one is responsible for the other.

## ETIOLOGY OF INTRA-ABDOMINAL AND MESENTERIC LYMPHADENITIS

Specific forms of intra-abdominal and mesenteric lymphadenopathy are commonly parts of distinct clinical complexes such as typhoid fever, dysentery, etc. The protean nature of the etiological factors concerned in nonspecific forms of lymphadenopathy within the abdomen is well shown by their relatively enormous distribution. Some are related to loosely gathered clinical entities known collectively as the "rheumatic" group. Still others are related to various groups associated with generalized cutaneous manifestations including some of the exanthemas. A large group seems to be related to a preceding "catarrhal" or "throat" infection, and this seems to have some relationship to forms of glandular fever and infectious mononucleosis and to what is clinically known as abdominal grippé. Finally there is a group in which the lymphadenopathy cannot be clinically connected with any demonstrable preceding or accompanying lesion. Because of the latter fact the cases in the latter group have been associated in a still undemarcated and undifferentiated classification and are for want of a better nomenclature called nonspecific mesenteric adenitis.

Not always is the causative agent demonstrable in nonspecific mesenteric adenitis. In only a minority of the latter cases bacteria can be demonstrated in the glands, and the predominating organism is some strain of streptococcus. Occasionally other bizarre organisms can be cultured such as *Bacillus melitensis*. An unidentified virus has also been suggested as the causative agent but the correlation of this virus with that which might cause poliomyelitis has not been proved. No relationship can be demonstrated by the Ix test with lymphogranuloma venereum. Various parasites have been found to occur in the intra-abdominal lymph nodes a causal relation cannot be established between them and acute nonspecific mesenteric adenitis, but in chronic mesenteric adenitis there might be some etiological connection in that the parasites might be intermediary factors in introducing other forms of bacterial infection.

factors may be accepted as more or less characteristic of this affection. It is difficult to say how frequent is this form of chronic lymphadenitis. In Foster's series of cases in which he has grouped acute and chronic cases, it seems remarkable that the percentage for the chronic cases is 64 as opposed to 8 per cent for the acute cases. My own experience is not large.

In the more advanced cases and in the group of older patients there is a tendency toward marked mimicry of other known symptom complexes there may be symptoms of dysphagia (Wakely) or symptoms suggestive of peptic ulcer (Thiemann, Lund Bler Keppeler and Erkes, Davidovitch Ljunggren Golden and Reeves) of biliary colic (Most, Pribram) of intestinal spasm (Schall) of constipation or diarrhea (Sternberg) of renal colic or hematuria (Schmieden Walker, Davidovitch, Golden and Reeves) or even of sciatica (Ljunggren). The commonest complex imitates very closely that which we customarily have known as "chronic appendicitis."

In this type of syndrome, more and more commonly as attention is being constantly focused on it, enlarged glands are the sole findings at abdominal explorations either performed frankly as such or done under mistaken diagnoses. Occasionally such glands are sufficiently large to be palpable before operation.

The differential diagnosis has commonly been most difficult in the chronic cases. Many factors must be considered, a general survey of which are

There are certain abdominal manifestations common in adults and practically unknown in infancy and early childhood, such as those of chronic gastritis, of ulcer and carcinoma of the stomach, of biliary colic, of gastric crises in tabes dorsalis, of movable kidney. Appendicitis is apparently very rare in the first and even the second year.

There are some abdominal syndromes that have the same significance and show the same characteristics at all ages, except perhaps in young children such as salpingitis, appendicitis, and renal colic.

3. Other abdominal manifestations occur wholly or predominantly in infancy or in early childhood. Nearly all of those occurring in infancy are produced by obstruction of a hollow viscus—pyloric stenosis, intussusception—or are associated with digestive abnormalities—colic. Later abdominal pain occurs with throat infections and with pneumonia but this is relatively rare. Chronic abdominal pain occurs with tuberculous spondylitis, with the chronic nonappendiceal forms of peritonitis, with tuberculous peritonitis, with rheuma-

tism and Henoch's purpura with the occasional case of worms, and lastly with enlarged inflamed mesenteric and retroperitoneal glands.

With modern methods and with adequate laboratory aid, it should not be difficult to make a differential diagnosis between urological, gall bladder stomach, and female pelvic disease. Cases of *bona fide* acute appendicitis in the vast majority of the cases should not escape one. In subacute and chronic cases of appendicitis, however the difficulties are great. The situation in regard to appendicitis may be summed up as follows:

a. The group in which delayed operation invariably resulted in cure. On these appendicectomy was not done in the acute stage of the various forms of a *bona fide* acute appendicitis. The symptoms continued for a variable length of time until a chronic phase was reached and the appendix was then removed. In such a case the usual condition found was a chronic abscess or a chronic hypertrophic appendicitis. In some cases the lesion resembled a nonspecific granuloma of the intestine.

b. A small group in which the pain resembled that of gastric and duodenal ulcer but was referred to the appendix despite the fact that no pathological lesion could be demonstrated therein. In almost countless experiences this has been proved to be a delusion: the pain has no demonstrable relation to the appendix or to the stomach and duodenum. It has no other demonstrable basis, and in practice such a pain is most difficult to handle as it does not react to any therapeutic agent employed.

c. A group in which appendicectomy and other forms of therapy failed to relieve episodes of pain or continuous annoying sticking pains in the right side of the abdomen, the symptoms simulating no well known complex.

In later years it has seemed to be more and more true that many if not all of the patients in groups b and c, had some form of psychoneurotic basis or background for the clinical picture. This conclusion was frequently confirmed by the presence of corneal and pharyngeal anesthesia and by excessive activity of the knee and other tendon reflexes.

d. A large group in which an obliterated appendix had previously been removed. Commonly removal was associated with somewhat hypertrophic change in the terminal nerves of the appendix, which was labeled a neurocema. Recurrence of symptoms was almost the rule and I am convinced that such anatomical changes are of a regressive involuntary character and cannot produce abdominal pain.

The differentiation between acute and chronic cases is sometimes more or less of an artefact, because at times the chronic cases are simply those in which a succession of acute episodes has taken place separated by intervals in which the symptomatology is less intense or in which it has simmered down even to the point where the symptoms are tolerated so completely as to make the patient believe they have disappeared entirely. In either case the chronic anatomical changes eventually characterize the pathological picture. This probably accounts for the peculiar percentage figures in Foster's series.

#### ROENTGENOLOGY

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Under the usual normal conditions, roentgenographic observation shows that the stomach empties continuously and barium passes steadily in the normal direction, reaching the cecum in  $1\frac{1}{2}$  to 4 hours. Each successive film shows progress distally in the position of the head of the barium column. The segmental peristaltic movements flow smoothly and are promptly followed by normal flexible relaxation of the intestinal wall. If there is no delay in movement, the ileum should be empty in 9 hours. The barium mass in the normal small intestine is usually continuous, that is, not broken up into separate small oval boluses. The width of normal, barium filled loops varies from 1.5 to 3.0 centimeters, and is usually 2.0 to 2.5 centimeters.

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## PORTAL OF ENTRY OF THE CAUSAL AGENT

The portal of entry for the causative agent of nonspecific mesenteric adenitis is only on rare occasions the appendix and this can happen only because of some anatomical abnormality of the lymphatic drainage pathways of the appendix. More commonly the portal of entry seems to be related to catarrhal or throat infections and then nonspecific mesenteric adenitis is least commonly a manifestation of a hematogenous mechanism or more commonly the causative agent is swallowed from the oropharynx and passed along to the terminal ileum from which local absorption occurs. Most frequent of all the nonspecific mesenteric adenitis is a local absorption effect from some local nondemonstrable lesion in the ileal segment of the alimentary canal. It can be safely assumed that this includes various forms of transient enteritis and other surface infections, various gross and microscopic injuries, and other forms of physical and chemical trauma.

In this most common mechanism the similarity to the ordinarily observed phenomena in cervical adenitis is absolute. In either case local injuries and infections permit the passage of the causative agent to the appropriate lymph nodes. The mechanism is based upon an exact duplication in either position of the anatomical arrangement of the local lymphadenoid tissue in the wall of the alimentary canal and of the corresponding lymph nodes. And the heaping up of extraordinary collections of lymphadenoid tissue in the wall of the alimentary canal at either of these locations is remarkable and seems important from an etiological and mechanistic viewpoint.

I wish to emphasize the importance of the terminal ileum as a regional portal of entry for the causal agent for many and perhaps most of the cases of simple nonspecific mesenteric adenitis. The opportunities for absorption of any causal agent are remarkable including that associated with the normal digestive functions and that predicated upon the occurrence of local points of injury. The passage of any provocative causal agent from the oral cavity to the terminal ileum is a constant occurrence and it is most remarkable that these forms of infection do not occur with greater frequency.

## THE LYMPHADENOID TISSUE

The important rôle played by the lymphadenoid tissue of the alimentary canal is only correctly appreciated when one realizes the great frequency with which it becomes involved in the various diseases known to clinical medicine. The tangible knowledge indicates an astonishingly large inci-

dence of involvement of the mesenteric glands in typhoid and paratyphoid fever in the various forms of bacteremia, in status lymphaticus, in tuberculosis, rarely in leues and actinomycosis, more commonly in the various blood dyscrasias, in a case of agranulocytosis reported by Felsen, and in the various forms of colitis, enteritis, and dysentery. This list does not include the various forms of malignancy and such borderline lesions as Hodgkin's disease. As indicated previously, in some of these, such as typhoid fever, the mechanism of development and of the transit of the infection is well known. The newer anatomical knowledge in colitis and dysentery indicates a fairly close approximation to the latter.

In all forms of diarrheal disease in infants and children—infantile diarrhoea, cholera infantum, acute ileocolitis in infants and children, summer diarrhoea, etc.—the process seems centered in or to show a predilection for the vicinity and substance of the intestinal lymphadenoid nodules and is especially marked in Peyer's patches. Apparently all of these forms begin as surface infections and reach down into the substance of the intestinal wall as the pathological process proceeds. The spread into the wall occurs along the lymph channels into collections of lymphadenoid tissue—solitary follicles, Peyer's patches. Wherever in the various publications (Holt, Felsen, etc.) particular attention is paid to this element and the findings recorded it is astonishing to see how much and how often other specific mention is made of the localization about and the involvement of Peyer's patches. In this regard the differentiation between small and large intestine is merely quantitative one and depends upon the distribution of solitary and aggregated collections of lymphadenoid tissue—solitary follicles—Peyer's patches. In the small intestinal cases, it is common to find the lesion localized for the most part or limited to the lower ileum where the lymphadenoid tissue abounds to such a large extent in the intestinal wall. The spread into and the involvement of the adjacent tissues of the intestinal wall becomes visible only with the prolongation of the illness and its anatomical development.

So-called catarrhal infections are commonly associated regionally with the upper reaches of the alimentary canal and have been previously referred to under the general nomenclature of throat infections. For the most part these occur anatomically in relation to the lymphadenoid apparatus of the tonsils and adenoids and their secondary involvements in the cervical glands. They are commonly said to be surface infections. Whether such catarrhal infections

can occur deep down in the ileum and originate in and about the Peyer's patches is something which is apparently beyond the present available powers of demonstration, but certainly it is so that in simple mesenteric adenitis without other demonstrable lesions there is identical symptomatic and anatomical manifestations to those similar lesions that originate in the oropharynx. The interplay of "throat" infection with abdominal symptoms as indicated in this communication is more than a mere coincidence and is remarkable.

#### INTRA-ABDOMINAL LYMPHANGITIS

Our entire conception and assumption regarding the clinical importance of intra-abdominal lymphangitis and lymphadenitis must be revised. Up to the present these have been accepted too lightly and in an indefinite way and have not been adequately correlated with the observable subjective and objective symptomatology.

Pribram's observations as to lymphangitis in the mesenterium will deserve attention. Pribram (1926) emphasized the occurrence of lymphangitic alterations strongly, and described the appearance of chronic lymphangitis in the mesenterium emanating from insignificant—possibly not even noticeable—inflammatory alterations in the intestinal wall. According to Pribram the altered lymphatic vessels in the mesenterium may be observed as strings, even of the thickness of the radial artery. Pribram considers that the glandular alterations he has observed, now as acute enlargements, now as cicatricial processes with peradenitis, play a less predominant symptomatic rôle than lymphangitis. Pribram's interpretation has followed the commonly accepted assumption that the appendix was at the bottom of the trouble, but he notes that even after appendectomy the process showed a tendency to successive spreading and occasional recrudescence, leading to shrinking of the mesenterium and diffuse adhesions in different parts of the abdominal cavity, owing to the spreading of the infection in the subserous lymphatic plexus. The lymphatic vessels of the portal fissure become infected in the same way, resulting in the pericholecystitis, periduodenitis, and possibly in a consequent spread of the infection to the pancreas. Pribram attaches great importance to the mesenteric alterations he describes. They are, he thinks, often the cause of discomforts after appendectomy in cases of chronic appendicitis and are a link with other more or less obscure abdominal affections, e.g., pancreatitis and peptic ulcer. Appendectomy and cholecystectomy, respectively, at an early stage are recommended also in clinically slight cases as prophylactic measures.

In spite of the fact that some of Pribram's conclusions are, perhaps, rather far fetched, his opinion regarding the clinical rôle and importance of intra-abdominal lymphangitis, and regarding the diagnostic importance of any residual anatomical alterations in connection with any preceding organic abdominal affection, should be well taken. Evidences of the latter abound on all sides, and I am sure that almost every operating surgeon can well remember many instances during a laparotomy in which evidences of preceding lymphangitis of greater or lesser extent were observed in the absence of other demonstrable lesions. As a matter of fact many of the instances in my own experience were explorations in which we were puzzled by the subjective symptomatology and the laparotomy was undertaken in an effort to find adequate cause and cure for the symptoms. Up to the present time these have been accepted, sometimes as being anatomical variations—adhesions—at other times as being evidences of some previous condition which we were too ready to accept as having no relation to the observed symptoms, but as one looks back upon his experience he can easily remember cases in which these areas directly connected with contiguous lesions in the bowel wall. To take an exaggerated example, a carcinoma or a diverticulitis of the sigmoid commonly presents visibly enlarged lymphatic channels and, in later cases, a secondary shriveling of the mesosigmoid, with enlarged palpable lymph nodes nearby. Nevertheless, it seems now that these opinions must be revised even if we are not quite ready to accept the assumption *in toto* that all of these patients suffer from such abdominal discomforts really suffer from some form of lymphangitis or adenitis. And in cases of this kind, the importance of the primary organic infection as a point of origin for any secondary lymphangitis and lymphadenitis must not be lost sight of as contributing in some part at least to the observable symptomatology.

#### PATHOLOGY

In acute cases intra-abdominal lymphadenopathy occurs (1) as part of a generalized adenopathy, (2) as an initial involvement of one group of glands with spread to other groups, and (3) as limited to one anatomically differentiated group of glands. Even though chronic adenopathies may begin in any of these ways, the rule is to find only one group of glands involved, although exceptions occasionally occur.

Evidences of any distinct inflammatory process are not always present in the glands which are removed for study. In general, all kinds of simple

hyperplasias and sinus catarrhal exudates are seen and in severe cases purulent fusions and frank abscess formation as well. In severe cases local and general forms of peritonitis occur either by transudation of infectious material or by perforation of glandular abscesses.

In the chronic cases the immediate impression is that lymph gland enlargement is due to some long standing—chronic—form of infection of immediately undeterminable etiological classification. The observable anatomical facts are frequently and commonly not easy to differentiate and classify. Commonly one questions the rôle of tuberculosis or one suspects an early stage of Hodgkin's disease or other form of lymphatic malignancy; or it may happen that one is not impressed with the presence of enlarged glands and dismisses them lightly as of no importance. And usually in the absence of any final conclusion the patient is referred to the follow-up clinic for further observation and study.

In both acute and, more commonly in the chronic cases giant cell systems are seen in the histological sections of some of the cases. Such giant cell systems or collections of epithelioid cells approach and are frequently indistinguishable from those of tuberculosis but the tendency to regress without excessive scarring and the absence of caseation and acid-fast bacilli in them, contradict this. They are usually found associated with severe infection of the alimentary canal accompanied by necrosis. Inasmuch as in the very much milder form of nonspecific adenitis only a hyperplastic condition is present in the lymph nodes, indicating a correspondence of intensity of process between the lymph node picture and the picture in the intestinal tract, it must be assumed that the differences in anatomical picture is caused by the different gradations of toxicity of the etiological cause or of the size and intensity of the dose of the causal agent which is delivered.

One must also assume that the so called tubercle arrangement can be found not only in specific forms of infection, like tuberculosis, and lues, but also in forms of nonspecific infection in which up to the present time no definite cause can be assigned. It might very well be that this sort of picture represents the anatomical progression between simple forms of lymphadenopathy on the one hand and those of definitely specific anatomical pictures, which are customarily correlated less often with lues and especially with tuberculosis. Undoubtedly this also explains the confusion which occurred, not only in the earliest historical period of this subject, but even in later times, in

classifying all forms of enlargement of the mesenteric glands as tuberculous.

Mixed infection in tuberculous adenitis plays a very important rôle. It is commonly noted in the neck. Less frequently it is observed in the abdomen. In such mixed infections the anatomical picture sometimes is vague enough to make it difficult to say definitely whether the infection is originally tuberculous even though from clinical experience we may feel fairly sure that it is. Mixed infection of tuberculous glands are commonly severe enough to cause sufficient destruction to wipe out a good deal of the glandular structure so that the original tuberculous formation cannot be visualized.

#### RELATIONSHIP OF TUBERCULOUS INFECTION TO ACUTE AND CHRONIC INFLAMMATORY ENLARGEMENT OF THE INTRA-ABDOMINAL LYMPH NODES

In many of these people there is a history of heavy exposure to tuberculosis in childhood, but at the time of examination evidences of tuberculosis are not obtainable either by physical examination or by laboratory tests. In girls there is sometimes more than the usual rise in temperature at the time of menstruation.

Physical examination generally shows thin nervous young woman with a temperature around 100 degrees F or less, and a tender abdomen. Sometimes an appendectomy has already been done at other times that is presented as the question at issue. Roentgenographic evidence of disease of the stomach, gall bladder and colon will not show anything abnormal, but occasionally calcified intra-abdominal lymph nodes are visualized.

Many an anatomical diagnosis of tuberculous mesenteric adenitis has been, and continues to be, made upon the roentgenographic demonstration of calcifications in the general region of the lower right abdominal quadrant. Pribram was of the opinion that glandular calcifications might set in as a final stage of any pathological process without having been preceded by a tuberculous infection. Noeske had also subscribed to the same opinion. In the former case, none of the observers had any method of establishing reliable proof except for the demonstration of the presence of tubercle bacilli which was frequently not valuable. In the latter group the contrariwise opinion was held because tubercle bacilli were not demonstrated and because of other clinical and collateral knowledge.

That inflamed and enlarged mesenteric and retroperitoneal glands, non-tuberculous in origin, do occur is well known. In his recent paper on

abdominal pain in children, Hutchison emphasized the importance of enlarged glands in the causation of abdominal pain in children

Personally, I am convinced from all of my experience, that although tuberculous infection is well known and has been adequately proved to exist in the mesenteric and other abdominal lymph nodes, there are also other cases of chronic inflammatory enlargement of these nodes with and without necrosis and with or without calcification, which are not caused by infection with the tubercle bacillus

#### COMPLICATIONS

The following complications have been reported in both acute and chronic intra-abdominal lymphadenitis (1) massive invasion of the entire lymphatic chain, (2) suppurative periadenitis with infiltration of the mesentery or with the formation of a tumor-like mass, (3) intra-abdominal abscess resulting from the rupture of a suppurative gland with or without local and general forms of peritonitis, (4) erosive bleeding from a large intra-abdominal blood vessel, (5) thrombosis of some vessel in the mesenteric plexus, (6) compression of a hollow viscus by enlarged inflamed glands, (7) intestinal obstruction, (8) obstruction of the biliary ducts, (9) compression of the ureter with secondary hydronephrosis

#### SUMMARY AND CONCLUSIONS

A number of concepts have resulted from this factual review

1 A very important common denominator of all of this aggregation of facts is the age factor. It is apparent that all of the conditions herein reviewed with which general and mesenteric lymphadenopathy is associated occur in the period of life beginning with childhood and extending with less frequency up to the adolescent period. It appears from this that during this period of life the lymphatic apparatus of the human being is under continual and variegated stress and is most apt to undergo pathological changes

2 The streptococci are most frequently associated with the various forms of so called non-specific lymphadenopathy and with the various clinically differentiated illnesses herein referred to. To be sure other organisms—staphylococci, diplococci, melitensis, etc.—are named even in conditions not specifically defined as a clinical disease such as typhoid fever, etc., but the predominating organism is the streptococcus. I am more and more impressed by the frequency with which causal agents of disease attack and enter the body through the upper end of the alimentary canal—oronasopharynx. There is a good deal of evidence

that the association of infection at the beginning of the alimentary canal—oropharyngeal cavity—with the abdominal manifestations centering in the general region of the terminal ileum is no mere coincidence. Corroboration of this is obtained in both experimental work (Poynton and Payne, and Adrian), and in clinical practice. Similarly, in the literature, reference has been made to the connection between appendicitis and an original oropharyngeal infection. I am also struck with the importance of an allergic mechanism in many of the previously mentioned conditions in which abdominal lymphadenopathy occurs. The rapid and abundant distribution of an exanthematic rash is probably based on an allergic distribution. In the visceral crises the edematous areas in the intestinal tract show remarkable similarities to external forms of angioneurotic edema and are undoubtedly indicative of a similar mechanism. Various forms of purpura commonly accompany the visceral crises. In the hyperacute fatal form of purpura there is indication of an overpowering biological mechanism, and no other branch of medicine comes so quickly to one's mind as that pertaining to allergic phenomena. Most probably the allergic antigen in any case is a bacterial product. Some of the phenomena remind one of histamine poisoning and histamine-like bodies are found commonly in the intestinal tract

3 The great facility with which generalized or mesenteric lymphadenopathies are associated with many apparently widely differing diseases indicates the great tendency for lymphatic absorption of these diseases during this period of life. It is practically impossible to obtain an accurate visualization of the general and ordinary condition of the enormous surface extent of the mucous membrane of the intestinal tract especially of the jejuno-ileum. It seems highly probable, nevertheless, that more frequently than one ordinarily imagines, there is some inflammation of this membrane, i.e., enteritis. There is every reason to believe that such inflammation can be responsible for many hitherto not sufficiently explained abdominal symptomatology, acute and chronic upsets in digestion, cyclic vomiting, etc., which are now thought to be "functional" in origin for many cases of diarrhea for which, at present, no adequate cause can be found, and for some other transient disturbances in the functions of the stomach and bowel, which so commonly accompany "colds" or "throat infections" or other generalized infections. Accurate correlation and integration of these symptomatology with the little and infrequently available knowledge obtained during postmortem examination is difficult. Com-

mon bacteriological causes for such transient and often unrecognized forms of enteritis may be the organisms or their toxins of the dysentery, enteritides, and colon groups of bacteria as well as staphylococci and streptococci. The studies of Childrey, Alvarez and Mann indicate that the digestive upsets that follow the eating of too much food or of undigestible food may well be due to injury wrought in this way to the absorptive power of the mucous membrane of the small bowel.

4. Intra-abdominal lymphadenopathy occurs under several basic conditions: (a) as an accompaniment or integral part of some definite disease such as typhoid fever, dysentery, etc.; (b) as a secondary manifestation to some intestinal lesion of more or less obscure origin such as nonspecific granuloma of the intestine; (c) as an incompletely understood accompaniment of indefinite groups of diseases usually associated with streptococci of one or another strain—the rheumatic group, for instance; (d) as a lymphadenopathy without any demonstrable or discoverable preceding causal lesion either nearby or at a distance that is, non-specific mesenteric adenitis.

5. The dominating position of the isolated and aggregated collections of lymphadenoid tissue at those points of the alimentary canal—oro-pharyngo-pharynx—where physiological activity and stress is normally at a maximum, where bacterial attack is most apt to occur where the products of bacterial attack and invasion are therefore most commonly developed and absorbed, neutralized without perceptible evidence or counteracted, blocked, and destroyed in the appropriate associated lymph nodes in the manifestations of disease. In intra-abdominal lymphadenopathy this corresponds to nonspecific mesenteric adenitis.

6. The great similarity in anatomy, physiology, etiology, mechanism and pathology between such forms of disease originating in the oropharynx and that originating in the lower ileum in either case lead to nonspecific forms of lymphadenopathy. This fact must be emphasized in order to wipe away any question of obscurity with which nonspecific mesenteric adenitis has been surrounded.

7. The similarity of the anatomical changes in the mesenteric nodes of the nonspecific type and those in the lymphadenopathies which occur in the other collateral or specific groups of diseases are reviewed herein.

8. In the great majority of the cases of nonspecific mesenteric adenitis it is not possible to prove any definite tuberculous etiology nor do the clinical facts give any reason for suspecting or

believing that the great majority of these conditions are tuberculous.

One must get away from the idea that mesenteric adenitis is some isolated bizarre peculiar or obscure disease. Rather one must understand that it has its counterparts in other lymphatic regional areas, that it is a sequel of other disease and infections, that it is a constant secondary phenomenon in many acute and chronic, mild and severe diseases of the intestinal tract, and that no one etiological factor or cause is responsible for the condition. This is not only my own opinion but has been pointed out also by Strombeck.

Inasmuch as in many cases abdominal lymphadenopathy is part and parcel of some larger definite clinical entity treatment must follow along the lines known by experience to be correct and adequate for the original disease. In nonspecific mesenteric adenitis and in the absence of any suppuration or other complication none but conservative treatment would be indicated if one could so perfectly diagnose the condition that the fear of an undiscovered acute appendicitis or other surgical emergency could be definitely eliminated. Unfortunately this is not possible at the present writing in clinical practice, and abdominal explorations are more or less frequently necessary in order to establish the true nature of the intra-abdominal condition.

#### BIBLIOGRAPHY

- ADOLPH, cited by Poynton and Payne.
- AL ARAB, W. C. Mesenteric lymphadenitis in adults, cause of appendicitis, indigestion, diarrhea and arthritis. *Med Clin N America*, 1930, 14, 605.
- BIER, A. *Funktionelle Bauchoperationen*. Deutsch. med. Wochenschr. 1902, 8, 535.
- CHILDREY, E. A., AL ARAB, W. C. and MANN, F. C. Digestion, efficiency with various foods and under various conditions. *Arch Int Med*, 1930, 40, 36.
- DAVIDOVITCH, S. Contribution à l'étude de la tuberculose des ganglions mésentériques. *Presse méd.*, 1926, 34, 6.
- DOA, CHARLES, A. Peripheral blood phenomena and differential response of bone marrow and lymph nodes to hyperpyrexia. *Radiology*, 1928, 10, 34.
- FELDMAN, JOSEPH. Acute and chronic bacillary dysentery. *Am J Path.*, 1930, 19, 204.
- Idem. Appendicular form of bacillary dysentery with notes on mesenteric adenitis and inflammation of distal portion of ileum. *Am J Dis Child*, 1935, 50, 66-67.
- FOSTER, A. K. J. Disease of the mesenteric lymph nodes; its relation to appendicitis, infections of the gastro-intestinal tract and granulomatous diseases: report of 3 cases. *Arch Surg*, 1935, 50, 28-3.
- FRIEDMAN, J. Surgical significance of mesenteric lymphadenitis. *Surg Gynec & Obst*, 1923, 37, 49.
- Idem. Chronic, non-specific enlargement of mesenteric lymph nodes as related to surgery. *Ann Surg*, 1929, 90, 6, 8-9.

- 12 GOLDEN, ROSS, and REEVES, R J The significance of calcified abdominal lymph nodes *Am J Roentgenol*, 1929, 22 305
- 13 GULEKE, E Die Hyperplasie der Mesenterial Lymphdruesen *Arch f klin Chir*, 1924, 133 517-532
- 14 HEUSSER, H Die Schwellung der mesenterialen Lymphdruesen *Beitr z klin Chir*, 1923, 130 85
- 15 HOLT, L EMMET Diseases of Infancy and Childhood New York and London D Appleton & Co, 1906
- 16 HUTCHISON, R Diagnostic significance of abdominal pain *Brit. M J*, 1921, 1 1
- 17 KEPPLER, W, and ERKES, F Diagnostische Irrtuemer bei Mesenterialdruesentuberkulose unter hesonderer Beruecksichtigung der Appendicitis *Med Klin*, 1919, 15 301
- 18 LJUNGGREN, C A Mesenterialkörteltuberkulosens forekomst hos skolbarn *Svenska Läkartidningen*, 1926, 23 1107
- 19 LUND Tuberculosis of the mesenteric glands simulat ing appendicitis *Boston M & S J*, 1912, 167 918
- 20 MOST A Chirurgie der Lymphgefäesse und der Lymphdruesen Stuttgart Ferdinand Enke, 1917
- 21 Idem Lymphbahnen der Bauchhoehle, in *Neue deutsche Chirurgie* No 24 41-47 Stuttgart Ferdin and Enke, 1917
- 22 NOESKE Lymphadenitis ileo-coecalis bei und nach Appendicitis *Zentralbl f Chir*, 1924, 51 2399
- 23 POYNTON, F J, and PAYNE, A A further contribu tion to the study of the etiology of appendicitis as a result of a blood infection, with particular reference to the tonsils as the primary seat of infection *Lancet*, 1912 (Aug)
- 24 PRIBRAM, B O Die Lymphangitis mesenterialis als abdominelle Herdinfektion, Substrat der peritonealen adhaesionen und Bindeglied zwischen den sogenannten zweiten Krankheiten *Arch f Chir*, 1930, 160 362
- 25 Idem Das Krankheitsbilder lymphangitis mesenterialis und peritonealis *Med Klin*, 1931, 27 871
- 26 Idem Umbilical colic, lymphangitic form of appendicitis and mesenteric lymphangitis *Muenchen med Wchnschr*, 1935, 82 942-944
- 27 SCHALIJ, J Calcification of mesenteric glands with intestinal spasm *Nederl Tijdschr v Geneesk*, 1928, 1 734
- 28 SCHMIEDEN Diagnose und operative Behandlung der Mesenterialdruesentuberkulose *Med Klin*, 1920, 16 219
- 29 SENNELS, A Hyperplasia glandularum mesenterii, adenitis meseraica *Ugesk f Laeger*, 1925, 87 1125
- 30 SHORT, A R Symptoms due to mesenteric lymphadenitis *Lancet*, 1928, 2 909-912
- 31 STERNBERG, A Zur diagnostik der Mesenterialdruesentuberkulose *Ztschr f Tuherk*, 1927, 47 117
- 32 STRÖMBECK, J P Mesenteric lymphadenitis, a clinical study *Acta Chirurg Scand*, 1932, 70 1
- 33 STRUTHERS, J W Mesenteric lymphadenitis simulat ing appendicitis *Edinburgh M J*, 1921, 27 22-26
- 34 THIEMANN, H Chirurgische Tuberculose der Mesenterial und Bronchialdruesen *Arch f klin Chir*, 1909, 91 245
- 35 WAKELY, C P G A case of calcified gland of unusual size giving rise to dysphagia *Brit J Surg*, 1922 10 295
- 36 WALKER, J T Relation of calcified abdominal glands to urinary surgery *Lancet*, 1922, 2 1213
- 37 WILENSKY, A O Mesenteric lymphadenitis *Med J & Rec*, 1920, 98 770
- 38 Idem Nonspecific granuloma of the intestine *Med J & Rec*, 1932, 135 445
- 39 Idem The essential nature of nonspecific granulomatous lesions of the gastrointestinal tract. *Surgery*, 1939, 6 288
- 40 Idem General abdominal lymphadenopathy, with special reference to nonspecific mesenteric adenitis *Arch Surg*, 1941, 42 71
- 41 WILENSKY, A O, and HAHN, L J Mesenteric lymphadenitis *Ann Surg*, 1926, 83 812-826

# EDITORIALS

## SURGERY Gynecology and Obstetrics

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### THE RÔLE OF CONSERVATIVE PROCEDURES IN TREATMENT OF SURGICAL EMERGENCIES

IT is of the utmost importance for the surgeon called on to perform emergency operations to realize that with each patient he faces two distinct major problems first, the saving of a life and, second, the correction of a pathological condition. Naturally their respective importance is in the order named, but because of zeal to effect a cure, it is sometimes easy to overlook the immediate problem at hand namely the preservation of life. For the latter often a temporary or palliative type of emergency operation will be sufficient to correct the physiological disturbance. After the patient's condition improves, radical corrective procedures can be undertaken with reasonable safety. The problem in emergency operations is entirely different from that presented by the patient with a more or less chronic ailment amenable to surgical treatment who being otherwise in good condition and electrolyte balance can be sub-

jected safely to the needed corrective operation usually at one stage.

Before any emergency operation likewise two other important problems should be solved if the surgeon is to give the patient the entire benefit of present knowledge and meet successfully the major problem that of preservation of life. These are first, an accurate pre-operative diagnosis and second, adequate pre-operative preparation. The diagnosis, surgical abdomen was often justifiable forty years ago but is permissible today only occasionally with the laboratory procedures, and stored blood and plasma which are now available to the surgeon. A few years ago the surgeon was forced to operate on patients in shock because intravenous infusions, blood and plasma were not available but with these agents at hand the patient's condition can be improved before operation and during these extra minutes or hours, as the case may be, an accurate diagnosis can be made. Certainly a patient who has pneumonia or coronary thrombosis is never improved by exploratory laparotomy and without a careful accurate diagnosis each can be mistaken readily at times for a "surgical abdomen." Likewise intravenous fluids in the quantity used in combating shock would only add to the gravity of the situation if administered to a patient following an acute coronary accident.

The value of intravenous fluids in cases of intestinal obstruction has been appreciated for almost two decades. It is not generally known, however that children and infants are especially vulnerable when subjected to surgical procedures when their fluid balance is poor. Also any patient who gives a history of vomiting or ileus should not receive an

anesthetic until a stomach tube has been passed and the stomach emptied of its contents

If all problems in emergency treatment were as direct as that of early uncomplicated acute appendicitis in which both the problems of urgency and cure are settled, there would be no excuse for this dissertation. Fortunately, the same is true in the majority of cases of acute cholecystitis, perforated peptic ulcer, strangulated hernia, ectopic pregnancy, and twisted or bleeding ovarian cyst. Because of the relative good condition of the patient, who has one of these lesions, life may be preserved and a cure effected at one operation. Unfortunately, some patients present a graver problem because of their poor condition, or the nature of their affliction, and a conservative procedure only must be performed that may or may not also result in cure of the pathological condition. This probably was first appreciated in the management of acute obstruction of the large bowel and it is now the accepted procedure, if the obstruction does not subside in a few hours after institution of conservative measures, to perform cecostomy or colostomy and to defer removal of the obstructing lesion until the obstruction is entirely relieved. This course allows time for evacuation and cleansing of the bowel, which is so important in the preparation for operations on the colon. Likewise, when an infant, an aged patient, or a patient in poor condition has a strangulated intussusception of the intestine, volvulus, or hernia, an exteriorization operation with proximal enterostomy as an emergency procedure gives a much greater hope of recovery than resection and a primary anastomosis. The intestinal continuity can be re-established with considerably less risk a few days later when the emergency is over. The fact that the intestinal obstruction is the item of first importance should be remembered in dealing

with strangulated hernia and not the herniorrhaphy

Any more radical procedure than simple closure of an acutely perforated peptic ulcer doubles the mortality rate. Since 80 per cent of patients remain well after this conservative procedure and usually medical regimen has not been tried, there seems to be little excuse for subjecting a patient in shock to gastroenterostomy or gastric resection. The effectiveness of medical regimen, which may be used to prevent further operation, is portrayed by patients with chronic duodenal ulcer. In these cases medical regimen almost invariably is advised and operation is required for relief in only about 15 per cent. In operating on the acutely inflamed gall bladder, the experienced surgeon will be able to accomplish cholecystectomy without difficulty in most instances. Occasionally, however, its removal will be hazardous because of the extent of the inflammation present or the poor condition of the patient. In such cases cholecystostomy can be performed unhesitatingly with the assurance that 85 per cent of such patients will not require cholecystectomy later. The management of perforation of the appendix with peritonitis is a controversial subject, but most surgeons who pursue an operative or radical policy become very conservative as soon as the peritoneal cavity is entered. Frequently, only drainage is instituted unless the appendix is free and readily accessible and the patient's condition warrants its removal. Great care is taken to prevent the breaking up of protecting or walling off adhesions. If a localized abscess shows no signs of resorption, it is drained, and if appendectomy is not accomplished at the primary operation its removal is recommended in the interval.

The gross mortality rate with emergent abdominal surgical procedures in experienced



hands is in the neighborhood of 10 per cent. The employment of preliminary conservative procedures in certain complicated problems could lower this figure appreciably.

JOHN M. WAUGH

## ADVANCES OF ABDOMINAL SURGERY IN INFANCY

THERE is probably no field of surgery that has been overlooked so much as that pertaining to infants and children. In fact, it is only within the past 5 to 10 years that any appreciable proportion of the medical profession has realized that the infant and child are subject to almost all the pathological conditions found in adult life plus many conditions never seen in the older age group. This change in point of view is strikingly evidenced by the great increase in the number of articles on children's surgery appearing in the leading medical journals and by the tremendous increase in the demand by young men for training in this field of surgery. Of course, with this increased interest in a particular phase of surgery there has been a marked improvement in the results obtained.

This improvement has been especially striking in the abdominal surgery of infants. It is interesting to recall that although congenital pyloric stenosis was well described by Beardsley as early as 1787 little or no attention was paid to the condition for well over a hundred years. Untold hundreds of infants must have died of this condition in the years intervening between then and the present day. In fact even in the very recent past the mortality remained over 50 per cent but today in well organized children's surgical clinics the mortality has dropped to a fraction of 1 per cent. This desirable change has come about by earlier recognition of the condition with an earlier diagnosis, by better preoperative prepara-

tion of the patient, by improved operative technique and by more intelligent postoperative care.

In 1916 Holmes made a careful examination of 120 pathological specimens of atresia of the bile ducts which showed that an appreciable number of these patients had ducts available for anastomosis to the bowel for any surgeon who wished to make the attempt. Yet it was not until 1927 that the first successful anastomosis of a congenital atresia of the bile ducts was performed. Since this first successful operation was performed at The Children's Hospital of Boston 6 other cases of atresia of the extrahepatic bile ducts have been successfully operated on and more than this number of cases of stenosis of the ducts have been relieved by surgical means. The relief in both groups has been permanent. It appears that over 30 per cent of the cases of congenital obstruction of the bile ducts are amenable to surgical relief and that in this group the operative mortality is not unduly high. It is surprising that there are not more successful results reported in the current literature.

Until very recent years the cure of a patient suffering from congenital atresia of the intestine was regarded as a surgical curiosity but reports of successful results are becoming much more common. Were it more generally appreciated that any infant who starts vomiting on the first day of life and continues to do so may be suffering from this condition, and were it also appreciated that the diagnosis can be simply and accurately made in the vast majority of instances, the successes would increase even more rapidly. A single x ray plate without the use of contrast media will not only suggest the diagnosis of intestinal obstruction but will often indicate the approximate site of the obstruction. The optimum time for performing these difficult anastomoses is within the first 48 hours of life. At this age infants

stand major surgical procedures extremely well. The mechanical difficulty of excessive distention has probably not taken place and gangrene of the bowel with perforation and peritonitis has not developed. It is still all too common for such infants not to be referred to the surgical clinic until they are *in extremis*. Of course, it must be recognized that special surgical technique is required for such cases, but this has already been developed in several clinics and should be developed in many more in the near future.

The intestinal obstruction due to faults of rotation, though often not complete and therefore not quite so urgent as the atresias, still present serious problems of early life. With our present knowledge of these conditions and the methods of surgical approach they can be effectively and permanently relieved in most instances.

In 1931 Hedblom showed that 75 per cent of infants having diaphragmatic hernia died before the end of the first month of life, and the mortality would be higher if the hernia through the esophageal opening had been excluded. If in newborn infants presenting symptoms of cyanosis, circulatory difficulty, or vomiting, the possibility of diaphragmatic hernia were more commonly considered, many fatalities from this condition could be avoided. Here again, as with the atresias of the bowel,

an x-ray examination without the use of contrast media will usually give an accurate diagnosis. When a diagnosis has been made of diaphragmatic hernia of major degree in the newborn infant, operation should be resorted to without delay. The policy of delay has yielded a mortality of over 75 per cent in the first month of life, whereas recognizing that the optimum time for surgical intervention is in the first 48 hours of life has reduced it tremendously. In the first two days of life the distention has not become marked and there is a better chance of being able to replace the abdominal viscera within the peritoneal cavity without undue pressure. When the tension of closing the abdominal wall is too great, a two stage closure has been proved to be a life-saving procedure. If this present plan of procedure is followed, it should be possible to reduce the present high mortality by 50 per cent or more.

These are but a few examples of the marked recent changes and advances in the field of abdominal surgery of infants. The knowledge of the pathological conditions which exist at this age, the development of suitable surgical technique, and the correct postoperative care of those small patients have also produced similar improvements in surgical conditions involving other parts of the body in newborn infants.

WILLIAM E. LEE

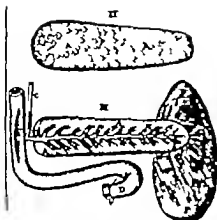


FIG. II.

AA The body of the Sweetbread detached in its natural form.

FIG. III.

The back-piece of the Sweetbread, together with the Spleen (marked with 'X').

AA The salivary glands of the Sweetbread, its blood-vessels being taken off.

XX The channel of the Sweetbread, widely spread out.

C The little pore opened to the channel.

DD A portion of the Great Duodenum, cut off.

E The common Orifice, by which the Salivary pore and channel of the Sweetbread, open conjointly into the Duodenum.

FFF The internal face of the Spleen.

GGG The veins and arteries distributed into the Spleen.

The Sweetbread (Pancreas) Glandular part of the Stomach, very profitable for concocting and purging the Chyle, and preparing it for the Liver and Spleen before be turned into blood, for so Nature directs each the blood is full, which either for nourishment of the true the veins, or to make the food for the Concoction of it, by ducts digress it first, even to the very back turns into blood, shows in the stomach, connects in the stomach, which is of consequence by the food, and by the force of the Sweetbread, from being and fatness, and therefore the Sweetbread is the one full of Chyle, as you may find it you select creatures alive, and cut the back.

Also there is a small oblong and singular channel in the Sweetbread, being filled out by our Physique, such as certain excretions (the Reticulum and flow of veins) It is much from the Gut called Duodenum, downwards in the extremity of the latter part, having common Orifice with an outward flow, connects with the latter part, from different place (separated completely in the Sweetbread with flow, yet very many branches) wide at the beginning, and continues by degrees before comes at the extremity of the Sweetbread. Stomach is suitable to man, but unusual in length, and arched over the latter part of being Superficial ducts.

The use of this channel is so much hard to be found out, for finding it brings certain Reticulum not unlike to the Gall, is superior the juice of several Mammals from the Chyle and carries away to the Gut Duodenum, and therefore that being stopped, the Sweetbread feeds by means of the excretions retained, and in many vessels being by the means suspended the Liver and Spleen receive no small damage.

Fig

Fig

Reproduced from Vesling Anatomy

On the Use of the Lay Term "Sweet Bread" for the Pancreas — 1 no B. Luckhardt



# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

THE book *Bacillary and Rickettsial Infections* by William H. Holmes<sup>1</sup> should have a wide appeal to those physicians and medical students who have a scholarly interest in disease. This volume takes up the large group of infectious diseases caused by bacilli and by rickettsia, namely the enteric infections, diphtheria, tetanus, gas gangrene, botulism, undulant fever, tularemia, plague, bereniosis, typhus, spotted fever, and a number of less important infections. The picture of each disease is presented against a rich historical background which gives the reader a sense of perspective. The development of our knowledge concerning the disease and its effect on human history are sketched in vivid terms. Consequently when the symptomatology and laboratory findings are discussed, one gets a splendid conception of the disease as a historical, clinical, and scientific entity. Dr Holmes' style is smoothly readable, his arrangement of material with comments in small type along the margins a useful one, and the profession owes him a debt of gratitude for introducing both scholarship and good literary style into sound medical writing.

The book was written as a textbook. The essential facts about the etiology, pathology and symptomatology of these infections are clearly presented, but these sections are not comprehensive enough to make the volume a useful reference work. Bacteriologists may well be disappointed by the small space devoted to bacteriology and immunology. Clinicians may feel that insufficient emphasis is placed upon differential diagnosis and treatment. If never the author did not set out to write a reference book, but rather an introduction to the study of medicine, or an orientation in medicine<sup>2</sup> as the publisher describes it. In this he has succeeded admirably. For the second year student in bacteriology Dr Holmes' book will give meaning to his long hours of laboratory work. If students in the third and fourth years take up the study of the infectious diseases with this book, they will gain a insight which can never come from mere study of the ordinary textbook. Later in their careers they may wish to consult the larger systems for information on specific points, but this volume will give them admirable understanding of the disease as a whole. Older physicians will find fascinating reading in these chapters, which will not only refresh and supplement their medical knowledge, but also kindle some of the enthusiasm of their student days.

Perhaps Dr Holmes should be commended most highly for the broad outlook on medical problems which he has skillfully woven into the text of his work. In the chapters on tuberculosis particularly, he has shown how closely the disease is interlarded with the social and economic problems of our society. This book sets the infectious diseases in their proper perspective in the field of medicine and human relations, and every medical student who aspires to be more than a mere craftsman should study this volume during the course of his training.

CHARLES A. J. KWA

Since this review was received, Dr Holmes passed away on November 2, 1940.

THE small textbook, *Practical Dermatology and Syphilis* by Robinson, is compact intended primarily for the medical student. It is a synopsis of most of the common skin diseases found in the average standard textbook of dermatology. Its purpose, perhaps, is much the same as that of the *Synopsis of Medicine* by Henry L. Tidy, namely to assist those who wish to review rapidly their knowledge of dermatology.

The general arrangement of the book follows that of the larger more comprehensive textbooks on the subject, and, while the subject matter is very briefly handled, in most cases the descriptions are adequate.

There are 430 photographs, but they are reduced so much in size that they fail to serve their purpose of giving the student an adequate picture of the disease. Then, too, they show many defects in lighting, depth, and sharpness of focus.

This book can only be recommended to beginners in dermatology as a primer, with emphasis on the warning of the author that for more comprehensive study and reference a more extensive textbook should be consulted.

EDWARD A. OLIVER.

THE thoritative monograph, *Lipid Metabolism of the Cellular Lipid Metabolism*<sup>1</sup> originally written as a section of *Oxford Lecture Notes in Medicine* includes studies on lipid metabolism begun 30 years ago by the author and his associates. The subject is presented in five parts: physiology and chemistry, hyperlipemia, xanthomatosis, Gaucher's disease, and Niemann-Pick disease. Clinical examples of the various conditions described are numerous and the

<sup>1</sup> PRACTICAL DERMATOLOGY AND SYPHILIS. By HARRY M. ROBINSON, M.D., Philadelphia. F. M. Robinson's Son & Co., Inc. 1940.  
<sup>2</sup> MEDICINE. OUTLINES OF THE CELLULAR LIPID METABOLISM. By Robinson, L. Thompson, M.D., Ph.D. Edited by Henry A. Christian, M.D., LL.D., Sc.D. (Hon.), F.A.C.P. New York: F. & T. Co. Reprinted from *Oxford Lecture Notes in Medicine*. London: New York: Oxford University Press, 1939.

GLACIARY AND ENTERIC INFECTIONS ACUTE AND CHRONIC.  
TEXTBOOK. BLACK SLATE TO WHITE PLASTER. By William H. Holmes.  
New York: The Macmillan Co. 1940.



role of alcohol is emphasized in explaining the recent increase in the number of cases of pellagra in cities.

In the foreword Dr. E. V. McCollum makes the following statement: "Nowhere else is so complete a history of investigations relating to pellagra, and the assembled quotations and comments make a fascinating story. Clinicians will be entertained and instructed by reading the views of their tedious col-

league, which point out how as the result of primary deficiencies, bodily conditions may through debility and derangement of function of the gastro-intestinal tract and the liver become unable to utilize indispensable nutrients in an adequate dietary. The book is a distinct contribution in that it extends the deficiency disease viewpoints beyond simple chemical reasoning into the field of perverted physiologic function."

HOWARD B. CARROLL.

## BOOKS RECEIVED

Books received are acknowledged in this department, and each acknowledgment must be regarded as sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

**SURGER OF MODERN WARFARE.** Edited by Hamilton Bailey, F.R.C.S. Vol. Baltimore: The Williams & Wilkins Co., 1911.

**PROCTOLOGY FOR THE GENERAL PRACTITIONER.** By Frederick C. Smith, M.D., M.Sc. (Med.), F.A.P.S. 1917 edition. Philadelphia: F.A. Davis Co., 1917.

**DIAGNÓSTICO DE LAS AFECIONES QUIRÚRGICAS DEL TÓRAX, PROCEDEMIENTOS TÉCNICOS QUIRÚRGICOS.** By Mario M. Brea and Jorge A. Talamá. Buenos Aires: El Ateneo, 1917.

**FRACTURES.** By George Perkins, M.C., M.Ch. (Oxon.), F.R.C.S. London and New York: Oxford University Press, 1910.

**THE HEART IN PREGNANCY AND THE CHILD-BEARING AGE.** By Burton E. Hamilton, M.D., and K. Jefferson Thomson, M.D. With section entitled "Delivery and Obstetrical

After Care of Caesarians." By Frederick C. Irving, M.D., F.A.C.S. Boston: Little Brown & Co., 1917.

**A PRACTICAL MANUAL OF DISEASES OF THE CHEST.** By Maurice Davidson, M.A., M.D. (Oxon.), F.R.C.P. (Lond.). Second edition. London and New York: Oxford University Press, 1917.

**THE PEDIATRIC COLOLOGY OF ADVERSE EFFECTS OF DRUGS.** By John A. Adair, M.D. Second Edition. Springfield, Ill. and Baltimore, Md.: Charles C. Thomas, 1917.

**ESSENTIALS OF DERMATOLOGY.** By Norman Tobias, M.D. Philadelphia, London, and Montreal: J.B. Lippincott Co., 1917.

**WAR WOUNDS AND INJURIES.** Edited by E. Fletcher, M.A., M.B., M.R.C.P., and R. W. Keen, F.R.C.S. Baltimore: The Williams & Wilkins Co., 1910.

**TEXTBOOK OF PEDIATRICS.** By J. F. Crowe Griffith, M.D., Ph.D., and A. Gessner Mitchell, M.D. Third edition. Philadelphia and London: W. B. Saunders Co., 1917.

**FIELD SURGERY IN TOTAL WAR.** By Douglas W. Jolly, M.B., Ch.B., M.C. New York: Paul B. Hoeber Inc., 1917.

## CORRESPONDENCE

### FAT EMBOLISM, A CLINICAL AND EXPERIMENTAL STUDY

To The Editor: In my article entitled "Fat Embolism: A Clinical and Experimental Study," published in the April 1918 issue of this journal, I stated on page 74:

"Decolin sodium (sodium dehydrocholate) has been recommended by Paul deLaen Chemical Company as a therapeutic agent in the treatment of fat embolism."

This statement should have read that Mr. Paul deLaen, president of Rhedel-de Laen Inc., made the

reference of decolin sodium, called my attention to the report by D. E. Rappert on November 7, 1918, and suggested that D. Rappert's work on fat embolism merited confirmation by further investigation.

I regret that my statement indicated that Mr. deLaen recommended decolin sodium as a therapeutic agent in the treatment of fat embolism. This was an error because, in Mr. deLaen's opinion, the available data are insufficient to justify its use in the treatment of this condition at the present time. I did not want to make a corporation of such slight reputation.

CARLO S. SCHUB

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

EVARTS A GRAHAM, St. Louis, *President*  
W EDWARD GALLIE, Toronto, *President-Elect*

*Committee on Arrangements*

LELAND S MCKITTRICK, *Chairman*, RICHARD H SWEET, *Secretary*

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## PRELIMINARY PROGRAM FOR 1941 CLINICAL CONGRESS

THE thirty-first annual Clinical Congress of the American College of Surgeons will be held in Boston November 3 to 7, when the fellows of this great medical center will sponsor a program of operative clinics and demonstrations covering all phases of surgical activity. The Congress has been held in Boston on several previous occasions, the first in 1915 and last in 1934. These meetings have made notable contributions to surgical and medical knowledge. Those who will attend in 1941 may anticipate a program of broad scope and interest, for the surgeons and clinicians of Boston have complete facilities at their command in the three medical schools and the thirty or more approved hospitals which will participate.

### CLINICAL PROGRAM

Under the leadership of a strong and representative Committee on Arrangements, plans are already under way for a complete and varied program for the five-day meeting. An extensive schedule of clinics and demonstrations is being arranged in the hospitals and medical schools which will, as usual, be the major feature of the Clinical Congress. Visiting surgeons will have every opportunity to obtain first hand information on a wide variety of surgical and related subjects as presented in the environment of excellent hospital facilities. In the operative clinics, surgical technique, use of operating room equipment, and organization of personnel will be demonstrated. Symposia and non-operative clinics will deal with the broader and equally important aspects of diagnosis, related non-surgical treatment, pre-operative preparation, and postoperative care, presented by means of discussion and through the demonstration of a wide variety of clinical material. Hospital diagnostic depart-

### COMMITTEE ON ARRANGEMENTS

|                      |                      |
|----------------------|----------------------|
| Leland S McKittrick  | William E Ladd       |
| Chairman             | Frank H Lahey        |
| Richard H Sweet      | Donald Munro         |
| Secretary            | Charles G Mixer      |
| Arthur W Allen       | Frank R Ober         |
| Edward D Churchill   | Robert B Osgood      |
| Howard M Clute       | George L Tobey, Jr   |
| E Granville Crabtree | Frederick H Verhoeff |
| Elliott C Cutler     | Irving J Walker      |
| Frederick C Irving   | Shields Warren       |

ments will offer important contributions in their respective fields. Specialists in varied fields, as well as surgeons, will participate in the discussions, so that many subjects will receive consideration from different viewpoints.

The medical schools and their affiliated hospitals have expressed a willingness to plan a series of exhibits demonstrating their work in clinical investigation and the latest advances in surgical research. These exhibits will be available for study in the local hospitals during the entire meeting. The basic science departments of the medical schools will present important work related to surgical practice. Thus, the Boston institutions will have much to offer in the way of a highly concentrated practical postgraduate course in surgery and allied subjects. A preliminary clinical program appears in the following pages. The preliminary clinical program as published at this time is incomplete in that a number of hospitals that will participate in the clinical program are not included. Schedules for the following hospitals will appear when the clinical program is again published: Lakeville State Sanatorium, New England Hospital for Women and Children, Newton, and St. Elizabeth's.

The program of each hospital is arranged to cover subjects in general surgery, obstetrics and gynecology, fractures, orthopedic surgery, thoracic



surgery, neurosurgery, genito-urinary surgery, ophthalmology and otolaryngology. Thus the visiting surgeon may select the clinics which he wishes to attend. Presentation of subjects under these classifications will be so correlated that he will have the opportunity to devote his time continuously to clinics dealing with the specialty in which he is most interested. The daily clinical bulletin will present the program according to the above classification. The complete detailed clinical program for the succeeding day will be posted each afternoon in the form of bulletins at headquarters in the Statler Hotel and distributed in printed form each morning. The preliminary programs and the general program to be published later will include as much detailed information as it is possible to present in advance, but it will be necessary for those who attend the Congress to make their clinic ticket selections from the daily bulletins.

#### SCIENTIFIC SESSIONS

The opening scientific session of the Clinical Congress, the combined presidential meeting and convocation, will be held on Monday evening in Symphony Hall. At this session the new officers of the College will be inaugurated and the initiates received into fellowship. Dr. Evans A. Graham, of St. Louis, will deliver the presidential address.

Eminent surgeons and specialists, recognized as authorities in their fields, will address the scientific meetings which will be held on Tuesday, Wednesday and Thursday evenings in the ballroom of the Copley Plaza Hotel. Special scientific meetings are being arranged for those who are interested in ophthalmology and otolaryngology on Tuesday, Wednesday and Thursday evenings. The Board of Regents of the College is giving careful attention to the selection of the speakers and subjects for these evening sessions, so that a well rounded program introducing the newest developments in general and special fields may be assured.

During recent years, at both the Clinical Congress and sectional meetings of the College, panel discussions held at the headquarters hotel have created unusual interest. Therefore, a schedule of thirty or more of these sessions is being planned for Monday, Tuesday, Wednesday and Thursday afternoons. These panels will be led by recognized authorities in each field who will have the aid of collaborators equally qualified to present fundamental facts on the chosen subject, and to direct the discussion in such a way that various viewpoints may be expressed. These sessions afford an opportunity for a large number of surgeons to participate and learn of the discoveries and experiences of others. The general plan

is for a ten-minute presentation of the subject by the leader, collaborators to follow with brief discussions on different phases of the topic, following which general discussion from the floor will be the final and major feature of each session.

Because of the widespread interest in the special subjects, a symposium on fractures and other traumas is being planned for one afternoon, and a symposium on cancer for another afternoon. As in former years, these sessions are expected to attract a large attendance.

A new feature introduced at the Clinical Congress in Chicago and which proved popular is again being planned for Friday afternoon. For these conferences ten special fields have been selected, and a pertinent subject of current interest will be briefly presented by a leader at each session. Discussion from the floor is directed by the leader and any surgeon attending is privileged to present a special problem related to the field under discussion with which he is concerned. Such opportunity for large groups of surgeons to participate in a consultation conference of this nature is apparently welcome.

The Board of Regents and the local committee aim to provide a varied type of program that will enable each individual surgeon to learn of the newer developments in many fields. The interests of both the general surgeon and the surgical specialists are being carefully considered in arranging all features of the program.

#### SPECIAL MEETINGS OF BOSTON SURGICAL SOCIETY

The Boston Surgical Society will hold a special meeting on the evening of Friday, November 7, in the ballroom of the Copley Plaza Hotel, to which all fellows of the College and other surgeons attending the Clinical Congress are invited to be present. The occasion of this special meeting of the society is the presentation of the Bigelow Medal to Dr. Allen O. Whipple, of New York, for his outstanding contributions to the advancement of surgery.

#### MEDICAL MOTION PICTURES

The visual education aspects of the program of the Clinical Congress will again be enlarged with the aid of medical motion picture films. The latest available pictures showing surgical procedures and related subjects will be exhibited. The schedule will be arranged so as not to conflict with either the clinical program at the hospitals or the scientific sessions, and will include both sound and silent, standard and color films which have been approved by the Committee on Medical Motion Pictures.

## HOSPITAL CONFERENCES

On Monday morning at 10 o'clock, in the Ballroom of the Copley-Plaza Hotel, the first session of the twenty-fourth annual Hospital Standardization Conference will open the Clinical Congress. At this session the 1941 list of approved hospitals, cancer clinics, and hospitals approved for graduate training in surgery and the surgical specialties will be officially announced. Dr. Evarts A. Graham, of St. Louis, president of the College, will preside. The hospital conference will continue on Monday afternoon in the same room, with sessions on Tuesday, Wednesday, and Thursday mornings, afternoons, and evenings. Programs are being arranged to interest hospital administrators, heads of various hospital departments and their personnel, nursing groups, and members of governing boards. One hospital conference in particular will be devoted exclusively to subjects of vital interest to members of governing boards. All aspects of the public relations problem will be discussed.

At a joint session with the Association of Record Librarians of North America, medical records will receive special consideration. National organizations representing various groups of hospital personnel will co-operate and participate in these meetings.

Some of the hospital conferences at the headquarters hotel will be formal sessions, others will be in the nature of panel discussions, round table conferences, and open forums. In certain sessions there will be a presentation of specific phases on a general theme by several speakers, in others a variety of subjects will be covered. The program will be developed to meet current needs, and from all indications is likely to emphasize from all angles the rôle of the hospital in the program of national defense.

As a special feature of the hospital conference it is planned to develop a program that will definitely appeal to the general surgeons and surgical specialists. This will take the form of a large general meeting with a series of panel discussions on appropriate subjects dealing with the care of patients, educational functions of the hospital, the control of surgery, and the clinical work in the related specialties. Organizations representing the specialty groups will be invited to participate in this phase of the program. Special consideration will be given in this series of meetings to the important subject of graduate training in general surgery and the surgical specialties. It is hoped that through this means the fellows of the College may become better acquainted with its extensive program of hospital activities which is

aimed at improvement in the environment in which the surgeon is working.

## PUBLICATION OF PROCEEDINGS

As in former years, the formal papers which are presented at the *scientific sessions* of the Congress will be presented in a special issue of the official journal of the College, *SURGERY, GYNECOLOGY, AND OBSTETRICS*, published in February following the meeting. This issue is furnished without additional charge to all fellows, junior candidates, and others who register for the Congress as invited guests. The papers which are presented in connection with the hospital standardization conference are published in subsequent issues of the *Bulletin* of the American College of Surgeons.

## ADVANCE REGISTRATION

The hospitals and medical schools of the Boston area afford accommodations for a large number of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the clinics. The limit of attendance will be based on a survey determining the available facilities in the participating hospitals and schools. It is expected, therefore, that surgeons who wish to attend the Congress will register in advance. A registration fee will be required in order to provide funds with which to meet expenses of the meeting. A formal receipt will be issued to each surgeon registering in advance, which will be exchanged for a general admission card upon presentation at headquarters during the Congress. This card, which is not transferable, must accompany all requests for clinic tickets and be presented for admission to the scientific sessions.

A resolution adopted by the Board of Regents provides that the registration fee for fellows of the College and endorsed junior candidates shall be \$5.00, that no fee for the 1941 Clinical Congress shall be required of initiates (class of 1941), that the fee for surgeons who are not fellows, attending as invited guests of the College, shall be \$10.00.

As in previous years, admission to clinics and demonstrations in the hospitals and certain of the scientific meetings at headquarters will be controlled by means of tickets. This plan provides for the distribution of visiting surgeons at the various clinics and other meetings, and helps to insure against overcrowding. The number of tickets issued for any clinic will be limited to the capacity of the room in which the clinic is held. Visiting surgeons are urged to co-operate in making the clinic ticket plan a success.

## HEADQUARTERS AND TECHNICAL EXHIBITIONS

Headquarters for the Congress will be established at the Statler and Copley Plaza Hotels where there are ample facilities for accommodating the Congress. All of the public rooms have been reserved for the exclusive use by the College during the five-day meeting. Registration for visiting surgeons and their ladies, the Technical Exhibition, executive offices of the College and certain scientific sessions and medical motion picture exhibitions will be located in the Statler Hotel. Registration for those attending the hospital conference, exhibits of College activities, and the morning, afternoon and evening hospital conferences will be located in the Copley Plaza Hotel. The evening scientific sessions on Tuesday, Wednesday and Thursday will also be held at the Copley Plaza.

The Technical Exhibition, registration desk for attending surgeons, clinic ticket and information bureau will be located in the ballroom on the mezzanine floor of the Statler Hotel. Additional space for the exhibition will be provided in the Assembly Room and the mezzanine lounge adjacent to the ballroom. Leading manufacturers of surgical instruments and supplies, sutures, dressings, pharmaceuticals, operating room equipment, x ray apparatus, hospital equipment of all kinds, and publishers of medical books will be represented in the exhibition. It will provide for the

visiting surgeons and hospital people an opportunity of carefully inspecting the finest modern products of all those industries which are helping to improve the service of hospitals and surgeons.

## BOSTON HOTELS AND THEIR RATES

In addition to the headquarters hotels, the Statler and Copley Plaza, there are a number of first-class hotels within a short distance of headquarters. These will provide ample facilities at reasonable rates. It is suggested that reservations for hotel accommodations be made well in advance of the meeting. The following hotels are recommended by the Committee

|                                      | Minimum Rates<br>with Bath |        |
|--------------------------------------|----------------------------|--------|
|                                      | Single                     | Double |
| Bellevue, Beacon Street.             | \$1 00                     | \$1 50 |
| Bradford, 75 Tremont Street.         | 1 00                       | 1 50   |
| Brunswick, 520 Boylston Street.      | 1 00                       | 1 00   |
| Rockminster, 645 Beacon Street.      | 90                         | 1 00   |
| Copley Plaza, 38 St. James Avenue.   | 4 00                       | 6 00   |
| Copley Square, 47 Huntington Avenue. | 75                         | 1 00   |
| Kenmore, 400 Commonwealth Avenue.    | 1 50                       | 3 00   |
| Lenox, Exeter Street.                | 1 00                       | 3 50   |
| Lincolnshire, 30 Charles Street.     | 1 00                       | 5 00   |
| Parker House, 60 School Street.      | 1 50                       | 5 00   |
| Ritz-Carlton, 1 Arlington Street.    | 5 00                       | 8 00   |
| Sheraton, 9 Bay State Road.          | 3 00                       | 5 00   |
| Somerset, 400 Commonwealth Avenue.   | 1 50                       | 6 00   |
| Statler Park Square.                 | 1 50                       | 5 00   |
| Towerne, 6 Boylston Street.          | 3 50                       | 5 00   |
| Vandome, 60 Commonwealth Avenue.     | 3 00                       | 4 00   |
| Westminster, 24 St. James Avenue.    | 90                         | 4 00   |

# PRELIMINARY CLINICAL PROGRAM

## MASSACHUSETTS GENERAL HOSPITAL

### Monday

#### GENERAL SURGERY

- H. K. BEECHER and associates—2 Dry clinic Anesthesia and related subjects  
 H K BEECHER—2 Anesthesia for transpleural gastric surgery  
 JULIA G ARROWOOD and H K BEECHER—2 10 Fractional spinal  
 H K BEECHER and R. A ADAMS—2 25 Use of ether in the presence of pulmonary tuberculosis  
 H K BEECHER—2 40 Anesthesia and shock  
 E B BENEDICT—3 30 Endoscopy, bronchoscopy and esophagoscopy with special emphasis on the two newer endoscopic methods, gastroscopy and peritoneoscopy, demonstration with lantern slides and patients  
 L S McKITTRICK and associates—2 Symposium Peripheral vascular clinic.  
 H. H. FAXON—2 Fundamental considerations, anatomy, physiology, etiology, examination  
 R. H THOMPSON—2 15 Late results following treatment uncomplicated varicose veins  
 H H FAXON—2 30 Present concept of treatment  
 R R LINTON—2 45 Chronic and recurrent ulceration of lower extremities, etiological factors and classification  
 R H ADAMS—3 05 High division and injection of long saphenous veins, division of communicating veins with and without excision of fascia, excision and graft, results  
 R R LINTON—3 30 Present concept of treatment  
 H H FAXON, R THOMPSON, R R LINTON, and R H ADAMS—4 Operations Peripheral vascular  
 Staff—2 Dry clinic Tumors

#### NEUROSURGERY

- J C WHITE and associates—2 Symposium  
 J C WHITE and J J MICHELSON—2 Operations  
 W J MIXTER—4. Electro-encephalographic control of anticonvulsant therapy  
 C S KUBIC and A O HAMPTON—4 Removal of lipiodol by lumbar puncture  
 J C WHITE—4 Effect of anesthesia on volume of brain

### Tuesday

#### GENERAL SURGERY

- A. W ALLEN and associates—8 Symposium Gastric lesions  
 C M JONES—8 Medical considerations  
 A O HAMPTON and associates—8 30 Roentgenological studies  
 E B BENEDICT—8 50 Gastroscopy and peritoneoscopy  
 C E WELCH—9 10 Gastric ulcer  
 LANGDON PARSONS—9 30 Cancer of the stomach  
 R H SWEET—9 50 Transthoracic gastrectomy  
 A W ALLEN—10 10 Surgical procedures for gastric lesions  
 Staff—10 30 Operative clinic Gastric resections for benign and malignant lesions  
 H H FAXON, HORATIO ROGERS, and associates—9-11 Symposium Acute appendicitis

- HORATIO ROGERS Present status, chief factors in present mortality rates, late diagnosis and/or treatment, faulty appraisal of individual patients, rigid policies of treatment, faulty technique, type of incision  
 W D SMITH Appendicitis in general medical practice  
 HORATIO ROGERS Appendiceal peritonitis before localization  
 H H FAXON Appendiceal peritonitis after localization  
 CHAMP LYONS The rôle of bacteriology and chemotherapy in appendicitis  
 R R LINTON Special aspects of appendicitis in young children  
 Staff—11 Operative clinic Acute appendicitis  
 L S McKITTRICK and associates—2 Symposium Cancer of colon and rectum  
 CHAMP LYONS and associates—2 Dry clinic Surgical infections

#### NEUROSURGERY

- J C WHITE and associates—9 Operative and dry clinic  
 W J MIXTER and J S HODGSON—9-11 Neurological operations  
 J C WHITE—11-1 Presentation of operative results in angina pectoris and extra pyramidal tremors  
 J J MICHELSON—11-1 Treatment of torticollis by alcohol injection of cervical muscles  
 J C WHITE and associates—2-4 Dry clinic  
 W J MIXTER Protrusion of nucleus pulposus in cervical spine  
 J S HODGSON Experience with cerebellar hemangiomas, Lindau's disease  
 J J MICHELSON Subdural abscess  
 W H SWEET New methods for measurement of blood flow  
 J C WHITE Spinothalamic tractotomy in the medulla

### Wednesday

#### GENERAL SURGERY

- L S McKITTRICK and associates—9 Operative and dry clinic Ulcerative colitis  
 C M JONES—9 Medical aspects, diagnosis and treatment.  
 L S McKITTRICK—9 20 Surgical aspects, types of operations and indications  
 JOHN D STEWART—9 40 Ileostomy, operative technique, postoperative complications  
 RICHARD H WARREN—10 10 Late results after ileostomy, social and economic aspects  
 L S McKITTRICK—10 30 Colectomy, indications, technique, results  
 Staff—11 Operative clinic  
 H C MARBLE and associates—9 Symposium Hand  
 H C MARBLE Anatomy and examination of the hand  
 F G BALCH, JR. Tumors of the hand  
 EDWARD HAMLIN, JR Injuries to nerves of upper extremity  
 W BRADFORD CANNON Skin grafts of the hand  
 A L WATKINS, A W REGGIO, and H C MARBLE Reconstruction of the hands, physiotherapy, occupational therapy, surgical reconstruction  
 A W ALLEN and associates—2 Symposium Diseases of the gall bladder and bile ducts  
 A W ALLEN—2 Technical considerations of the gall bladder and bile ducts with special reference to morbidity and mortality

- RICHARD H. WALLACE—30. Acute cholecystitis  
JOHN D. STEWART—35a. Obstructive jaundice, liver function, preparation of the patient, and after-care.  
RICHARD H. WALLACE—35b. Carcinoma of the gall bladder.  
Staff—35c. Operations. Extra-hepatic biliary tract.  
L. S. McKEITHEN and associates—2. Symposium. Peripheral vascular disease.  
L. S. McKEITHEN—2. Fundamental considerations, classification, differential diagnosis.  
EDWARD HAMILT, JR.—5. Thrombo aneurysm obliterans. Outline of treatment, nerve cranking mechanical aids, indications for amputation.  
H. E. KEYWARD—15. End result study. With particular reference to the economic aspect of the disease.  
RICHARD H. WALLACE—35. Arteriovenous aneurysms with and without diabetes. Indications for and technique of minor amputation.  
T. C. PRATT—3.10. Indications for and technique of supracondylar amputation.  
R. H. SMITH—3.30. Lumbar sympathectomy. Its role in the treatment of obliterative disease. Indications for operation and operative technique.  
Staff—4. Operations. Supracondylar amputation for gangrene, nerve cranking for relief of pain, lumbar sympathectomy.

#### GENITO-URINARY SURGERY

- G. G. SMITH and associates—9. Operative and dry clinic.  
Staff—9. Operations.  
F. H. COLE—30. Genito-urinary tuberculosis.  
RICHARD CRUTE—30. Results of treatment with estrogenic substances in prostatic hypertrophy.  
B. B. KELLEY—10. Complications of transurethral resection.  
LEONARD WOODRUFF—40. The female urethra.  
G. G. SMITH and associates—2. Operative and dry clinic.  
Staff—2. Operations.  
G. G. SMITH—3.30. Treatment of prostatic cancer.  
ARTHUR WILLIAMS—3.50. Chronic prostatitis.  
W. F. LEONARD—4. a. Renal arteriography.  
JOHN P. GIBBS—4.30. The male hormone.

#### THORACIC SURGERY

- E. D. CHURCHILL and associates—0. Symposium. Primary tumors of the lung and mediastinum.

### Thursday

#### GENERAL SURGERY

- A. W. ALLER and associates—8. Symposium. Duodenal ulcer.  
C. M. JONES and associates—8. Medical considerations.  
A. O. HAMPTON and associates—8.30. Roentgenological diagnosis.  
E. B. BENDER—8.30. Gastroscopy gastritis.  
A. W. ALLER—9.1. Surgical considerations.  
HOWARD ULLMANN—9.40. Acute perforation.  
C. E. WELCH—10. a. Malfunction of anastomotic stoma and after-care.  
Staff—10.30. Operations.  
V. H. KARLOVIAN—8—30. Operative and dry clinic. Plastic surgery, presentation of cases operated upon for various deformities.  
L. S. McKEITHEN and associates—0. Operative and dry clinic. Acute small bowel obstruction.  
RICHARD H. WALLACE—0. Physiological aspects of non-stimulation obstruction, cause of death.  
L. S. McKEITHEN—20. Factors influencing mortality rate.

- S. P. BAKER—40. Diagnosis.

RICHARD H. WALLACE—37.10. Non-operative treatment, practical considerations in the use of Miller Abbott tube.

L. S. McKEITHEN—2.30. Résumé, outline of treatment, results.

Staff—4. Operations.

#### GENITO-URINARY SURGERY

- G. G. SMITH and associates—9. Operative and dry clinic.  
G. G. SMITH and associates—9. Operations.  
HOWARD L. SCHUB—30. The solution of urinary calculi.  
RICHARD CRUTE—10.30. Problems in the treatment of urinary calculi.  
F. H. COLE—5. Deep x-ray therapy in cancer of the bladder.  
S. B. KELLEY—40. Ureterostomy versus nephrostomy.

#### THORACIC SURGERY

- E. D. CHURCHILL and associates—0. Symposium. Septic diseases of the lung.

#### ORTHOPEDIC SURGERY

- M. V. SMITH PETERSEN and associates—0. Operative and dry clinic.

### Friday

#### GENERAL SURGERY

- E. D. CHURCHILL and associates—9. Operative and dry clinic. Parathyroid tumors.  
L. S. McKEITHEN and associates—2. Symposium. Peripheral vascular disease.  
RICHARD H. WALLACE—2. Fundamental considerations of thrombus formation, clinical manifestations, diagnosis and treatment.  
H. H. FAYON—30. Pulmonary embolism, its relation to venous thrombosis.  
RICHARD H. WALLACE—45. Use of heparin in prevention of pulmonary embolism.  
C. E. WELCH and C. E. MCGARREY—3. Venography. Indications, technique, results.  
H. H. FAYON—37.5. Exploration and division of the femoral vein, indications and operative technique.  
C. E. WELCH—3.35. Results, early and late after division of the femoral vein.  
H. H. FAYON, C. E. WELCH, and RICHARD H. WALLACE—4. Operations.  
R. H. SMITH PETERSEN and associates—0. Symposium. Surgery of hypertension, non-nephritic.  
ROBERT S. P. LEE. Statement of the problem.  
BENJAMIN CASTLEMAN. Renal pathology.  
JOHN H. TALBOT. Renal physiology.  
RICHARD CRUTE. Urological factors.  
R. H. SMITH PETERSEN. Modification of abnormal physiology by sympathectomy.

#### OBSTETRICS AND GYNECOLOGY

- J. V. MORGAN and associates—9. Symposium. Gynecological problems.  
J. V. MORGAN, LAMOND PARKS, and MARSHALL E. BAILEY—9—30. Operations.  
J. V. MORGAN and associates—10.30—Discussion and demonstrations.

#### ORTHOPEDIC SURGERY

- M. V. SMITH PETERSEN and associates—9. Operative and dry clinic.

## BOSTON CITY HOSPITAL

*Monday*

## GENERAL SURGERY

## Staff—2 Symposium Vascular diseases

- E E O'NEIL Refrigration in gangrene of lower extremities  
 E A EDWARDS Thrombophlebitis in unusual forms  
 S J G NOWAK Experimental hypertension  
 D C GOLDFARB False aneurysm of femoral artery  
 T LEARY Pathological aspects of vascular disease  
 E E O'NEIL Lumbar sympathectomy for vascular disease

*Tuesday*

## GENERAL SURGERY

## Staff—2 Dry clinic

- W R MORRISON Gastrojejunocolonic fistula  
 C W MCCLURE Gastroscopy, Kodachrome pictures  
 I C WALKER Bleeding peptic ulcers  
 A R KIMPTON Cancer of stomach.  
 W R MORRISON Perforated peptic ulcer  
 E E O'NEIL Transpleural approach for carcinoma of upper end of stomach  
 T W WICKHAM Cholecystitis and its relation to peptic ulcer

## OBSTETRICS AND GYNECOLOGY

## Staff—2 Symposium Pregnancy, the physiological and pathological aspects

- GEORGE R MINOT and EUGENE L LOZNER The hemorrhagic diatheses complicating pregnancy  
 FREDERICK J LYNCH Treatment of miscarriage  
 FREDERICK PARKER, JR Pathology of toxemia of pregnancy with especial reference to changes in the placenta  
 CARM R ALDEN Disorders of the urinary tract encountered in obstetrics  
 BENEDICT F BOLAND Hormonal relationship between the kidneys and toxemia of pregnancy  
 MAXWELL FINLAND Pneumonia in pregnancy

## FRACTURES AND OTHER TRAUMAS

## OTTO J HERMANN and associates—9 Symposium Fractures of the ankle

- OTTO J HERMANN Introduction  
 GORDON M MORRISON Simple unilateral ankle injuries with fracture  
 JOSEPH BURNETT, G G BAILEY, JOSEPH SHORTELL, and RUSSELL SULLIVAN Complicated ankle fractures, bilateral, following Cotton's therapeutic ankle classifications Slides, charts, individual cases, and apparatus illustrate various points in this symposium

## OPHTHALMOLOGY

## JAMES J REGAN and staff—9 Symposium Abnormal fundi

## OTORHINOLARYNGOLOGY

## Staff—9 Dry clinic

- H. F. FRIEDMAN Septic thrombophlebitis of frontal veins, with abscess formation  
 E J MONAHAN A method for the extirpation of branchial cysts  
 OSCAR HIRSCH Surgical removal of pituitary tumor via transnasal route  
 LOUIS M. FREEDMAN Bronchoscopic treatment of pulmonary atelectasis

- CHESTER R. MILLS Osteomyelitis of the frontal bone  
 BENJAMIN RISEMAN Gumma of nasopharynx and lung  
 SAMUEL W. GARFIN Treatment of fractures of the jaw  
 PHILIP E. A. SHERIDAN, CHARLES DEWOLFE, and FREDERICK HEDMLICK Presentation of cases

*Wednesday*

## GENERAL SURGERY

## Staff—9 Dry clinic

- Department of Pathology Splenogenic myeloid metaplasia, argentophil tumors (carcinoid)  
 DR JOLIFF Surgical treatment of myeloma  
 F W O'BRIEN Cancer and x ray therapy  
 E A COONEY Carcinoma of breast.  
 A R KIMPTON Cancer of large intestine  
 CHARLES LUND Cancer of mouth  
 I C WALKER Cancer of stomach  
 Staff—2 Symposium Thyroid disease  
 R C COCHRANE Tumors of parathyroid with lantern slides  
 D D BERLIN Hyperthyroidism with cancer of thyroid  
 W T SALTER Graves' disease without hypertension  
 RICHARD SMITH Adenoma of thyroid  
 R C COCHRANE Complication of thyroidectomy

## Staff—2 Symposium Vitamins in surgery

- CHARLES LUND and J H CRANDON Vitamin C and wound healing  
 WALTER WEGNER and MERRILL MOORE Vitamins in presence of head injuries  
 DR MIKELJOHN Presentation of cases

## Staff—2 Symposium

- GORDON M MORRISON Radial nerve injury with fracture of humerus  
 J E FLYNN Anatomical and clinical investigations of deep fascial space abscess of the hand  
 T K RICHARDS Traumatic injuries of the knee joint  
 J E FLYNN Dupuytren's contracture  
 A P AITKEN Epiphyseal separation  
 J E FLYNN Treatment of traumatic lesions of the hand  
 ROBERT ULIN Club feet

## OBSTETRICS AND GYNECOLOGY

## Staff—9 Dry clinic

- Speaker to be announced Anesthesia and analgesia with special reference to spinal and intravenous anesthesia  
 DR REGINALD and R D MARGESON Placenta previa in patients previously delivered by low transverse cesarean section  
 FREDERICK L GOOD Physiology of lower uterine segment  
 DANIEL J MCSWEENEY Radiographic pelvimetry  
 Staff—9 Dry clinic  
 F W O'BRIEN Results in treatment of carcinoma of the uterus in the tumor clinic of a general hospital  
 FREDERICK PARKER, JR and JOHN T WILLIAMS Pathology of so-called fibrosis of the uterus

*Thursday*

## GENERAL SURGERY

## OTTO J HERMANN and associates—9 Symposium Low back pain

- OTTO J HERMANN Introduction  
 JOHN T WILLIAMS Gynecological aspects  
 AUGUSTUS RILEY Genito-urinary aspects  
 ROBERT ULIN A rational method of routine back examination based on anatomical and physiological factors  
 JOSEPH SHORTELL Low back pain with negative x rays,

- RICHARD H. WALLACE—30. Acute cholecystitis  
JOHN D. STEWART—30. Obstructive jaundice, II or  
function, preparation of the patient, and after-care.  
RICHARD H. WARREN—315. Carcinoma of the gall  
bladder  
Staff—330. Operations Extra-hepatic biliary tract.  
L. S. McKITTERICK and associates—2. Symposium. Peri-  
hepatic vascular disease.  
L. S. McKITTERICK—2. Fundamental considerations,  
classification, differential diagnosis  
EDWARD HAMILTON, JR.—5. Thrombo-angitis obli-  
crum. Outline of treatment, nerv. crushing, mechan-  
ical aids, indications for amputation.  
H. E. KENNARD—33. End-result study. Ith particular  
reference to the economic aspect of the disease.  
RICHARD H. WARREN—35. Arterio-sclerotic gangrene  
with and without diabetes. Indications for and tech-  
nique of minor amputation.  
T. C. PRATT—330. Indications for and technique of  
supracondylar amputation.  
R. H. SHERRICK—330. Lumbar sympathectomy, its  
role in the treatment of obliterative disease. Indica-  
tions for operation and operative technique.  
Staff—4. Operations. Supracondylar amputation for  
gangrene, nerv. crushing for relief of pain, lumbar  
sympathectomy.

## GENITO-URINARY SURGERY

- G. G. SMITH and associates—9. Operative and dry clinic  
Staff—9. Operations.  
F. H. COLEY—30. Genito-urinary tuberculosis  
RICHARD CURTIS—50. Results of treatment with  
estrogenic substances in prostatic hypertrophy  
S. B. KELLEY—Complications of transurethral  
resection.  
LOUISE WOODRUFF—40. The female urethra  
G. G. SMITH and associates—2. Operative and dry clinic  
Staff—2. Operations.  
G. G. SMITH—330. Treatment of prostatic cancer  
ARTHUR WILLIAMS—330. Chronic prostatitis  
W. F. LEONARD—470. Renal arteriography  
JOHN P. GIER—430. The male hormone

## THORACIC SURGERY

- E. D. CRITCHFIELD and associates—9. Symposium. Pri-  
mary tumors of the lung and mediastinum

## Thursday

## GENERAL SURGERY

- A. W. ALLEN and associates—8. Symposium. Duodenal  
ulcer.  
C. M. JONES and associates—8. Medical considerations  
V. O. HURSTON and associates—830. Roentgenological  
diagnosis.  
E. B. BEVERIDGE—830. Gastroscopy gastritis  
A. W. ALLEN—9.10. Surgical considerations  
HOWARD UHLENHUTH—940. Acute perforation  
C. E. WELCH—Malfunction of anastomotic stoma  
and after-care.  
Staff—30. Operations.  
V. H. KAZANJE—830. Operative and dry clinic.  
Plastic surgery presentation of cases operated upon for  
various deformities.  
L. S. McKITTERICK and associates—Operative and dry  
clinic. Acute small bowel obstruction.  
RICHARD H. WARREN—Physiological aspects of non-  
strangulation obstruction, cause of death.  
L. S. McKITTERICK—30. Factors influencing mortality  
rate

- S. P. SARRIS—40. Diagnosis  
RICHARD H. WARREN—3. A. Non operative treatment,  
practical considerations in the use of Miller Abbott  
tube.  
L. S. McKITTERICK—330. Review, outline of treatment  
results.  
Staff—4. Operations

## GE TO-URINARY SURGERY

- G. G. SMITH and associates—9. Operative and dry clinic  
G. G. SMITH and associates—9. Operations  
HOWARD I. SEELY—30. The solution of urinary calculi  
RICHARD CURTIS—50. Problems in the treatment of  
urinary calculi  
F. H. COLEY—5. Deep x-ray therapy in cancer of  
the bladder  
S. B. KELLEY—40. Ureterostomy versus nephro-  
tomy

## THORACIC SURGERY

- E. D. CRITCHFIELD and associates—Symposium. Sep-  
purative disease of the lung.

## ORTHOPEDIC SURGERY

- M. N. SMITH, PATTERSON and associates—Operative and  
dry clinic.

## Friday

## GENERAL SURGERY

- E. D. CRITCHFIELD and associates—9. Operative and dry  
clinic. Parathyroid tumors  
L. S. McKITTERICK and associates—Symposium. Peri-  
hepatic vascular disease.  
RICHARD H. WARREN—2. Fundamental considerations of  
thrombus formation, clinical manifestations, diagnosis  
and treatment.  
H. H. FAXON—30. Pulmonary embolism, its relation  
to acute thrombosis.  
RICHARD H. WARREN—45. Use of heparin in preven-  
tion of pulmonary emboli.  
C. E. WELCH and C. E. McGARRY—3. Venography indi-  
cations, technique results.  
H. G. FAY—33. Exploration and division of the  
femoral vein, indications and operative technique.  
C. E. WELCH—33. Results, early and late, after divi-  
sion of the femoral vein.  
H. H. FAY, C. E. WELCH, and RICHARD H. WARREN—  
4. Operations.  
R. H. SHERRICK and associates—Symposium. Surgery  
of hypertension, non-nephritic.  
ROBERT S. P. LACK. Statement of the problem.  
BRYANT CASTLEMAN. Renal pathology.  
JOHN H. TALBOT. Renal physiology.  
RICHARD CURTIS. Urological factors.  
R. H. SHERRICK. Modification of abnormal physiology  
by sympathectomy.

## OBSTETRICS AND GYNECOLOGY

- J. V. MILES and associates—9. Symposium. Gynecolog-  
ical problems.  
J. V. MILES, LANGDON PARKER, and MARSHALL E.  
BARTLEY—930. Operations.  
J. V. MILES and associates—30. Discussion and  
demonstrations.

## ORTHOPEDIC SURGERY

- M. N. SMITH, PATTERSON and associates—9. Operative and  
dry clinic.

## PETER BENT BRIGHAM HOSPITAL

*Tuesday*

## GENERAL SURGERY

- ELLIOTT C CUTLER and ROBERT E GROSS—9 Operations Ligation of patent ductus arteriosus, pericardiectomy
- ELLIOTT C CUTLER and associates—10 Symposium Surgery of the heart and blood vessels
- C SIDNEY BURWELL Forms of heart disease amenable to surgery
- SAMUEL A LEVINE Cardiac disease simulating surgical conditions of the abdomen and vice versa
- EUGENE C EPPINGER Indications for surgery for patent ductus arteriosus
- ROBERT E GROSS Surgical treatment of patent ductus arteriosus
- ELLIOTT C CUTLER The technique of pericardiectomy
- MERRILL C SOSMAN The rôle of the roentgenologist in cardiac surgery
- JOHN HOMANS Peripheral vascular disease
- MARSHALL N FULTON Angiomas of skeletal muscle.
- DAVID CHEEVER—2 Dry clinic Surgical anatomy of the abdomen

*Wednesday*

## GENERAL SURGERY

- ELLIOTT C CUTLER and ROBERT ZOLLINGER—9 Operations Gastric resections
- ELLIOTT C CUTLER and associates—10 Symposium Gastric and duodenal ulcer
- ELLIOTT C CUTLER Indications for surgery with gastric and duodenal ulcer
- EDWARD S EMERY, JR Medical management of bleeding peptic ulcer
- MERRILL C SOSMAN Significance of prepyloric ulcer
- HARRY A WARREN Duodenal diverticulum
- ROBERT ZOLLINGER Surgical treatment of severe duodenal ulcer
- ELLIOTT C CUTLER Results of acute gastroduodenal perforation
- CARL W WALTER—2 Symposium Aseptic technique

*Thursday*

## GENERAL SURGERY

- FRANCIS C NEWTON and J ENGLEBERT DUNPHY—9 Operations Colon, rectum and anus
- ELLIOTT C CUTLER and associates—10 Symposium Colon, rectum and anus
- FRANCIS C NEWTON Experiences with cancer of the colon
- J ENGLEBERT DUNPHY Experiences with anterior resection for cancer of the rectosigmoid
- ANDREW W CONTRATTO and THOMAS B QUIGLEY Differential diagnosis of gastritis and gastro-enteritis from appendicitis
- MERRILL C SOSMAN The x ray and large bowel surgery
- EDWARD S EMERY, JR Medical diseases of the colon
- ELLIOTT C CUTLER Cicatrizing enteritis

## GENITO-URINARY SURGERY

- WILLIAM C QUINBY and associates—2 Symposium
- J HARTWELL HARRISON The diagnosis and treatment of common injuries of the urinary tract
- GEORGE AUSTEN A correlation of the clinical aspects and pathology of the fused renal mass

- G PHILIP GRABFIELD Renal blood flow
- F ANTHONY SIMONE Experimental hypertension
- WILLIAM C QUINBY A critical evaluation of prostatic surgery in recent years

*Friday*

## GENERAL SURGERY

- ELLIOTT C CUTLER and ROBERT ZOLLINGER—9 Operations Cholecystectomy, choledochostomy
- ELLIOTT C CUTLER and associates—10 Symposium Surgical diseases of the biliary tract
- ELLIOTT C CUTLER Biliary calculus, technique of surgical therapy
- MERRILL C SOSMAN Upright films of the gall bladder as an aid in the diagnosis of cholelithiasis
- ROBERT ZOLLINGER Acute cholecystitis
- THOMAS B QUIGLEY Surgery of the biliary tract in the aged
- WILLIAM A DAVIS Clinical use of vitamin K in surgery of the biliary tract
- EDWARD S EMERY, JR Medical treatment after cholecystectomy
- ELLIOTT C CUTLER and associates—2 Symposium Surgical treatment of hyperthyroidism
- ELLIOTT C CUTLER The domain of thyroid surgery
- SAMUEL A LEVINE Pre-operative and postoperative treatment of severe thyrocardiacs
- MARSHALL N FULTON Recurrent hyperthyroidism
- J ENGLEBERT DUNPHY Use of silk in surgery of the thyroid
- HARRY B FRIEDGOOD Rôle of the pituitary hormone in thyrotoxicosis
- ELLIOTT C CUTLER Technique of thyroidectomy

## BOSTON LYING-IN HOSPITAL

*Tuesday*

## OBSTETRICS AND GYNECOLOGY

- Staff—10 Operative and dry clinic
- CHARLES A JANEWAY Treatment of puerperal sepsis with sulfanilamide and immune transfusions
- CLEMENT A SMITH Effect of various anesthetics as shown by blood gas determinations on mothers and their infants

*Wednesday*

## OBSTETRICS AND GYNECOLOGY

- Staff—2 Dry clinic
- MEINOLPH V KAPPIUS The rôle of soft tissue x ray technique in the diagnosis of placenta previa
- ROBERT N RUTHERFORD Interpretation of bleeding in the first trimester of pregnancy as shown by endometrial biopsies
- ARTHUR T HERTIG Pathological ova, chief cause of spontaneous abortion
- ROBERT H BARKER Determination of cephalopelvic disproportion by the Thoms method of roentgenometry

*Thursday*

## OBSTETRICS AND GYNECOLOGY

- Staff—10 Operative and dry clinic
- JOHN L NEWELL External cephalic version as prophylaxis against the fetal hazards of breech presentations
- DANIEL ABRAMSON End results of a conservative policy at delivery as shown in a study of postpartum patients



## Friday

## GENERAL SURGERY

## Staff—s. Symposium

- C. G. SERRIN. Chemotherapy in general peritonitis.  
 MAXWELL FINLAND. Chemotherapy in surgery.  
 R. H. ALDERMAN. The dynamical treatment of hernia. *With special reference to shock.*  
 H. G. DEXTER. "Z" plastics in hernia.

## THORACIC SURGERY

## Staff—g. Symposium

- J. W. STEINBERG. Suppurative pericarditis, colored motion pictures, partial empyema, result of modern method of treatment, lobectomy for bronchiectases.  
 HORACE BURNETT. Methods and results of treatment of pulmonary tuberculosis.  
 S. J. G. NOWAK. Experimental pulmonary embolus.  
 DR. SEUTZ. Intratracheal anesthesia for thoracic surgery.

## ORTHOPEDIC SURGERY

## Staff—p. Symposium. Fractures of the hip

- NEWTON C. BROWDER. Intracapsular fractures of the hip.  
 ROWELL SULLIVAN. Hip fractures, cases of operation, reduction and internal fixation.  
 OTTO J. HERRMANN. Partial un-united hip fractures.  
 THOMAS H. PETERSON. Posterior fusion of the hip.  
 A. A. THOMPSON. Shipped femoral epiphysis.  
 JAMES W. SEVER. Presentation of cases.

## FREE HOSPITAL FOR WOMEN

## Tuesday

## OBSTETRICS AND GYNECOLOGY

## Staff—p. Symposium. Carcinoma of the cervix

- FRANK A. PENDERBTON—g. Operation. Radium application.  
 ARTHUR T. HERRING and F. CL. A. YOCUM—g-ga. Drug deaths of early carcinoma.  
 P. CL. A. YOCUM— Management of the uterological complications.  
 GEORGE VAN S. SMITH—10-30 Results.

## Wednesday

## OBSTETRICS AND GYNECOLOGY

## Staff—g. Symposium. Cancer of the endometrium

- FRANK A. PENDERBTON—g. Operation. Hysterectomy for carcinoma of endometrium.  
 ARTHUR T. HERRING—g. Pathology.  
 GEORGE VAN S. SMITH— 30 Results.

## Thursday

## OBSTETRICS AND GYNECOLOGY

- GEORGE V. S. SMITH, JOSEY ROCK, and associates—g.  
 Symposium. Fertility hormones in gynecology.

## Friday

## OBSTETRICS AND GYNECOLOGY

## Staff—g. Symposium. Tumors of the ovary

- GEORGE VAN S. SMITH—g. Operation. Cancer of ovary.  
 ARTHUR T. HERRING— Pathology.  
 FRANK A. PENDERBTON— 45 Results.  
 SIDNEY C. GRAVER— Kraurosis of the vulva.

lumbar, sacro-iliac, myositis, myositis-fasciitis, bacterial postural, mechanical findings.

THOMAS H. PETERSON. Coccygodynia, fracture of coccyx, conservatism vs. surgery in treatment.  
 ROWELL SULLIVAN. Anatomical abnormalities of the fifth lumbar vertebra and lumbosacral joint.  
 G. KIVVETHE COOKE. Spontaneous thoracic Pathology, diagnostic points, role of trauma in its production, and treatment.

A. P. ATKIN. Facial contractions.

MARK H. ROOKES. Orthopedic aspect, Intervertebral disc problem.

P. F. BUTLER. Intervertebral disc problem, -my aspect.  
 DONALD McVIE. Intervertebral disc problem, neurological aspect.

Staff—s. Symposium. Appendicitis, biliary system, and hernia.

P. S. FOWLE. Appendicitis and complications.

G. W. PAPER. Incision for appendectomy in extreme obesity.

T. W. WICKHAM. Analysis of 600 cholecystectomies.

F. F. HENDERSON and JOHN McGOWAN. Operative biliary drainage for relief of jaundice: operative cure of gall bladder patient.

J. J. HERRMAN. Functional hemolytic jaundice and splenectomy.

W. R. MORRISON. Stones of the hepatic ducts: sub-diaphragmatic abscess.

CHARLES LAMM. Peritoneoscopy. *With special reference to biliary disease.*

RICHARD SMITH. Exteriorization of small intestines in strangulated hernia.

D. C. GORDON. Recurrent inguinal hernia.

Staff—s. Symposium. Anesthesia, large intestine, and other abdominal surgery.

T. W. WICKHAM. Foci of infection and ulcerative colitis.

A. R. KINGTON. Surgery of large intestine.

J. EDWARDS F. THOMAS. Abdominoperitoneal resection of rectum for carcinoma. *With abscess formation.*

C. W. McCLELL. Sigmoidoscopy, kiodachrome pictures.

FRANK MARVIN. Indications and contra indications for various anesthetics.

S. C. WYCKOFF. Spinal anesthesia.

G. C. MOORE. Intravenous anesthesia.

P. S. FOWLE. Ruptured corpus hemorrhagicus.

ALLEN D. VIL. Calcified cyst of spleen.

S. J. MADDOCK. High and low intestinal obstruction.

ALLEN DAVIS. Gun shot wounds of abdomen.

HARLEY B. LODGE. Postoperative treatment.

## GENITO-URINARY SURGERY

Staff—g. Symposium

H. H. HOWARD. Epidermoid carcinoma of the penis.

GEORGE C. PRATER. Stricture of the urethra.

S. R. MUELLER. Newer concepts of urinary extravasation.

G. D. ANDERSON. Scrotal plastics after klopaphic gynecology.

W. H. HOLTHAM. Treatment of gonorrheal urethritis with sulfathiazole.

J. A. SIEK. Removal of calculi from lower ureter by the vaginal route. *Report of cases.*

F. G. SERRIN. Fracture of the penis, case report. Anatomical study of remnants of prostatic tissue in the prostatic bed following castration.

ARTHUR RILEY. Hemangioma of kidney. *Case report.*

## OPHTHALMOLOGY

JAMES J. RICE and staff—g. Operations

## ORTHOPEDIC SURGERY

G E HAGGART and J W TOUMEY, JR —9 Operations

## OTORHINOLARYNGOLOGY

WALTER B HOOVER—9 Operations

F D LATHROP—1 30 Operations

WALTER B HOOVER—1 30 Dry clinic Local anesthesia in surgery of nose and throat, method used in tonsillectomy, adenoidectomy, lingual tonsillectomy, and excision of lateral pharyngeal bands, septum, sinus surgery including Caldwell Luc, external frontal, intranasal surgery, plastic procedures on external nose, disease of the esophagus, summary of symptoms, diagnosis and treatment of carcinoma, esophageal diverticulum, cardiospasm, esophagitis, ulcers, strictures of esophagus, and perforation, thyroid disease in the larynx, laryngeal paralysis

## NEW ENGLAND BAPTIST HOSPITAL

*Monday*

## GENERAL SURGERY

H D ADAMS and N W SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract

U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations Anesthesia

## THORACIC SURGERY

H D ADAMS—1 30 Operations

## NEUROSURGERY

GILBERT HORRAX—1 30 Operations

## OTORHINOLARYNGOLOGY

F D LATHROP—1 30 Operations

*Tuesday*

## GENERAL SURGERY

F H LAHEY, R B CATTELL, S F MARSHALL, and B P COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract.

U H EVERSOLE, LEO V HAND, and M J NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general

H D ADAMS and N W SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract.

U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations Anesthesia

## GENITO URINARY SURGERY

E E EWERT and VERNON S DICK—9 Operations

## THORACIC SURGERY

H D ADAMS—1 30 Operations

## NEUROSURGERY

J L POPPEN—9 Operations

GILBERT HORRAX—1 30 Operations

## ORTHOPEDIC SURGERY

G E HAGGART and J W TOUMEY, JR —9 Operative clinic

## OTORHINOLARYNGOLOGY

WALTER B HOOVER—9 Operations

F D LATHROP—1 30 Operations

*Wednesday*

## GENERAL SURGERY

F H LAHEY, R B CATTELL, S F MARSHALL, and B P COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract

U H EVERSOLE, LEO V HAND, and M J NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general

H D ADAMS and N W SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract.

U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations Anesthesia

## GENITO-URINARY SURGERY

E E EWERT and VERNON S DICK—9 Operations

## THORACIC SURGERY

H D ADAMS—1 30 Operations

## NEUROSURGERY

J L POPPEN—9 Operations

GILBERT HORRAX—1 30 Operations

## ORTHOPEDIC SURGERY

G E HAGGART and J W TOUMEY, JR —9 Operative clinic

## OTORHINOLARYNGOLOGY

WALTER B HOOVER—9 Operations

F D LATHROP—1 30 Operations

*Thursday*

## GENERAL SURGERY

F H LAHEY, R B CATTELL, S F MARSHALL, and B P COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract

U H EVERSOLE, LEO V HAND, and M J NICHOLSON—9 Anesthesia demonstrations Regional, spinal, continuous spinal, and general

H D ADAMS and N W SWINTON—1 30 Operative clinic Thyroid, stomach, colon, rectum, and biliary tract

U H EVERSOLE, LEO V HAND, and M J NICHOLSON—1 30 Demonstrations Anesthesia

## GENITO-URINARY SURGERY

E E EWERT and VERNON S DICK—9 Operations

## THORACIC SURGERY

H D ADAMS—1 30 Operations

## NEUROSURGERY

J L POPPEN—9 Operations

GILBERT HORRAX—1 30 Operations

## ORTHOPEDIC SURGERY

G E HAGGART and J W TOUMEY, JR —9 Operative clinic

## OTORHINOLARYNGOLOGY

WALTER B HOOVER—9 Operations

F D LATHROP—1 30 Operations

*Friday*

## GENERAL SURGERY

F H LAHEY, R B CATTELL, S F MARSHALL, and B P COLCOCK—9 Operative clinic Thyroid, stomach, colon, and biliary tract.

## NEW ENGLAND DEACONESS HOSPITAL

*Monday*

## GENERAL SURGERY

H. D. ADAMS and N. W. SWINTON—30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—30. Demonstrations and symposium: Anesthesia.

## THORACIC SURGERY

H. D. ADAMS—2. Operations.

## NEUROSURGERY

GILBERT HOBBAK—30. Operations.

## OTORHINOLARYNGOLOGY

F. D. LATROFF—30. Operations.

*Tuesday*

## GENERAL SURGERY

F. H. LARKY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCLOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.  
H. D. ADAMS and N. W. SWINTON—30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—30. Demonstrations: Anesthesia.  
F. H. LARKY, LEWIS M. HUNTEN, ELMER C. BASTELD, and H. J. PERKIN—Dry clinic: Symposium on thyroid surgery.

## GENITO-URINARY SURGERY

E. E. EWERT and VERNON S. DICK—9. Operations.

## THORACIC SURGERY

RICHARD H. OVERBOLT and R. H. BETTS—9. Dry clinic.  
H. D. ADAMS—30. Operations.

## NEUROSURGERY

J. L. POWPES—9. Operations.  
GILBERT HOBBAK—30. Operations.

## ORTHOPEDIC SURGERY

G. E. HADGART and J. W. TOOMEY, JR.—9. Operations.

## OTORHINOLARYNGOLOGY

WALTER B. HOOVER—9. Operations.  
F. D. LATROFF—30. Operations.

*Wednesday*

## GENERAL SURGERY

F. H. LARKY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCLOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.  
H. D. ADAMS and N. W. SWINTON—30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—30. Demonstrations: Anesthesia.  
R. B. CATTELL, N. W. SWINTON, and EVERETT D. KIEFER—2. Dry clinic: Symposium on colon and rectal surgery.

## GENITO-URINARY SURGERY

HARVARD H. CRANTEE—9. Operations.  
E. E. EWERT and VERNON S. DICK—9. Operations.

## THORACIC SURGERY

H. D. ADAMS—30. Operations.

## NEUROSURGERY

J. L. POWPES—9. Operations.  
GILBERT HOBBAK—30. Operations.

## ORTHOPEDIC SURGERY

G. E. HADGART and J. W. TOOMEY, JR.—9. Operations.

## OTORHINOLARYNGOLOGY

WALTER B. HOOVER—9. Operations.  
F. D. LATROFF—30. Operations.

*Thursday*

## GENERAL SURGERY

F. H. LARKY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCLOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.  
H. D. ADAMS and N. W. SWINTON—30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—30. Demonstrations: Anesthesia.  
F. H. LARKY, SARA M. JORDAN, and S. F. MARSHALL—Symposium on gastric, duodenal, and jejunal surgery.

## GENITO-URINARY SURGERY

E. E. EWERT and VERNON S. DICK—9. Operations.

## NEUROSURGERY

J. L. POWPES—9. Operations.

## ORTHOPEDIC SURGERY

G. E. HADGART and J. W. TOOMEY, JR.—9. Operations.

## OTORHINOLARYNGOLOGY

WALTER B. HOOVER—9. Operations.

*Friday*

## GENERAL SURGERY

F. H. LARKY, R. B. CATTELL, S. F. MARSHALL, and B. P. COLCLOCK—9. Operative clinic: Thyroid, stomach, colon, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—9. Anesthesia demonstrations: Regional, spinal, continuous spinal, and general.  
H. D. ADAMS and N. W. SWINTON—30. Operative clinic: Thyroid, stomach, colon, rectum, and biliary tract.  
U. H. EVERSOLE, LEO V. HAYD, and M. J. NICHOLSON—30. Demonstrations: Anesthesia.

## GENITO-URINARY SURGERY

E. E. EWERT and VERNON S. DICK—9. Operations.

## THORACIC SURGERY

RICHARD H. OVERBOLT and R. H. BETTS—Dry clinic.  
H. D. ADAMS—30. Operations.

## NEUROSURGERY

J. L. POWPES—9. Operations.  
GILBERT HOBBAK—30. Operations.

## BETH ISRAEL HOSPITAL

*Tuesday*

## GENERAL SURGERY

Staff—9 Dry clinic

ARNOLD STARR Biliary tract disease, left sided pain  
C G MIXTER Technique of immediate cholangiography motion pictures

A L HERMANSON Cholangiography, indications for and end results

H A FRANK Advantages of intravenous synthetic vitamin K over other vitamin K preparations

A M SELIGMAN Vitamin P in capillary fragility

Staff—10 30 Operative clinic

C G MIXTER Cholecystectomy and cholangiography

JACOB FINE Cholecystectomy, transverse incision

L H NASON Peritoneoscopy, spinal anesthesia

ARNOLD STARR Peritoneoscopy, local anesthesia

Staff—2 Dry clinic

MAX DAVIS Ovarian tumors with endocrine effects

R B DAVIDOFF Relationship of cystic disease of the breast to disease of the uterus and adnexa

A L HERMANSON Comparative merits of the vaginal smear and endometrial biopsy in diagnosis of ovarian function

S L GARGILL Hyperparathyroidism

D D BERLIN Carcinoma of the thyroid

M F LESSES Complications of thyroid surgery

S L GARGILL Management of recurrent and persistent thyrotoxicosis

D D BERLIN The avoidance of complications in thyroid surgery

## GENITO URINARY SURGERY

Staff—9 Dry clinic

I G CRABTREE Pre-operative preparation of prostatic cases

G C PRATHER and M L BRODNY Accessory bladder pathology in prostatic cases

G C PRATHER and DR REICH Accessory renal pathology in prostatic cases

F G CRABTREE Summary of 12 years' experience in prostatic surgery

G C PRATHER Results of contact therapy for bladder tumors

I G CRABTREE—10 45 Operation Bladder tumor, contact radiation therapy

Staff—2 Dry clinic

E L PRIE Adaptation of the Trätner hydrophorograph for bladder studies

DR ZIMMERMAN Bladder atonies

J H LIFTON Bladder atonies as demonstrated by the Trätner hydrophorograph

S R MULLNER Testosterone effect on bladder tone, diabetic atony of the bladder

B L GREENBERG Value of cholinergic and adrenergic drugs in bladder atonies

H A KONTOFF Rate of recovery of bladder after relief of obstruction

S R MULLNER Stress incontinence in the female

I L PRIEN Crystallography of the sulfonamide drugs

*Wednesday*

## GENERAL SURGERY

Staff—9 Dry clinic

I H NASON Pressure treatment of keloids

J B SEARS Prophylaxis of pulmonary embolism by division of femoral vein

Oscar HIRSCH Changes in volume of the peritoneal cavity following intercostal nerve paralysis

C G MIXTER Giant hernia

ARNOLD STARR Advanced regional ileitis

C G MIXTER Transverse ileocolostomy with or without resection for regional ileitis

Staff—10 30 Operative clinic

C G MIXTER Intestinal resection

J B SEARS Division of femoral vein for treatment of non fatal pulmonary embolus

D D BERLIN Thyroidectomy

Staff—2 Dry clinic

M D ALTSCHULE Obstruction of the superior vena cava

B ALEXANDER Blood bank

MAX DAVIS and SAMUEL GILMAN Venous pressure changes in lower extremities during and after abdominal surgery

S B BEASER Rare earth anticoagulants

JACOB FINE Thrombophlebitis and embolism, diagnostic and therapeutic considerations

B ALEXANDER Polycythemia vera in peripheral vascular disease

B F MASSELL and S B BEASER Evaluation of therapy of peripheral vascular disease

JACOB FINE Adrenal cortical hormones in shock and hemorrhage

*Thursday*

## GENERAL SURGERY

Staff—9 Dry clinic

S S HANFLIG Use of traction in treatment of cervical arthritis

M H ROGERS Treatment of acute subdeltoid bursitis by needling, novocain and irrigation, mechanics of fracture of surgical neck of humerus, methods of reduction

ARMAN KLIN Chemotherapy of acute sepsis of bones and joints

DR RHEINGOLD and W S ALTMAN Delayed roentgenological evidence of fracture

M H ROGERS Intervertebral disc, orthopedic aspects

W JASON MIXTER Intervertebral disc, neurological and surgical aspects

DAVID AYMAN Results of sympathectomy for hypertension

Staff—10 30 Operative clinic

R H SMITHWICK Sympathectomy for hypertension

W JASON MIXTER Removal of intervertebral disc

M H ROGERS Manipulation for chronic adhesive bursitis

Staff—2 Dry clinic

ALFRED HURWITZ Sulfanilamide vs zinc peroxide in the treatment of phagedenic ulcer

LOUIS ZITZLL The Miller Abbott tube

M D ALTSCHULE Effect of abdominal surgery on respiratory dynamics

H L BLUMGART The surgical risk in cardiac patients

JACOB FINE Treatment of intestinal distention by sulfaguanidine

ARNOLD STARR Sulfaguanidine for the sterilization of isolated loops of colon

## GENITO-URINARY SURGERY

Staff—9 Dry clinic

I L PRIEN A new method for stone analysis

D B STEAFNS Parathyroid disease and urinary lithiasis

G C PRATHER Roentgenology of the kidney at operation

- U. H. EVERSOLE, LEO V. HARR, and M. J. NICHOLSON—*g.*  
Anesthesia demonstrations. Regional, spinal, continuous  
spinal, and general.  
H. D. ADAMS and N. W. SWINERTON—*g.* Operative clinic  
Thyroid, stomach, colon, rectum, and biliary tract.  
U. H. EVERSOLE, LEO V. HARR, and M. J. NICHOLSON—  
*g.* Demonstrations. Anesthesia.

## GENITO-URINARY SURGERY

- E. L. EWERT and VERNOR S. DICK—*g.* Operations.

## THORACIC SURGERY

- H. D. ADAMS—*g.* Operations

## NEUROSURGERY

- J. L. POFFEY—*g.* Operations.  
GILBERT HERRICK—*g.* Operations.

## ORTHOPEDIC SURGERY

- G. E. HAGGARD and J. W. TOWNLEY, JR.—*g.* Operative  
clinic.

## OTO-RHINO-LARYNGOLOGY

- WALTER B. HOOVER—*g.* Operations.  
F. D. LATIMER—*g.* Operations.

## PALMER MEMORIAL HOSPITAL

## Monday

## GENERAL SURGERY

- Staff— Symposium. Carcinoma of the breast.  
CLIFFORD C. F. VERNER. End-results of surgical treat-  
ment.  
L. S. McKEITHEN. Interstitial irradiation treatment  
of carcinoma of the breast. 5th platinum radium  
needles.  
J. H. MARRAS. X-ray therapy of carcinoma of the  
breast.  
SHIELD PARKER. Relation between chronic cystic  
mastitis and carcinoma of the breast.

## Tuesday

## OBSTETRICS AND GYNECOLOGY

- G. A. LELAND, JR. and C. J. SWAN—*g.* Symposium. Treat-  
ment of carcinoma of the cervix.

## Wednesday

## GENERAL SURGERY

- Staff— Symposium. Carcinoma of the rectum and anus.  
L. S. McKEITHEN. Choice of operation in cases of  
carcinoma of the rectum.  
W. F. LEADREITER. Urological complications after  
resection of the rectum.  
L. S. McKEITHEN. Treatment of carcinoma of the rectum  
in poor risk cases with electrocoagulation and radium  
implantation.  
J. H. MARRAS. X-ray therapy of carcinoma of the rectum.  
R. H. SWERT. Carcinoma of the anal canal.  
R. H. SWERT or CLIFFORD C. FRANKLIN. End-results of  
treatment of carcinoma of the rectum.

## Friday

## GENERAL SURGERY

- Staff— Symposium. Diabetic gangrene.

## H. F. ROOY. Medical aspects.

- L. S. McKEITHEN. Principles of surgical treatment,  
classification of lesions, conservative methods.  
T. C. PRATT. Indications for and technique of major  
amputation.  
L. S. McKEITHEN. Indications for and technique of  
major amputation.  
T. C. PRATT. End-result study of 100 patients after  
supracondylar amputation for gangrene.  
L. S. McKEITHEN and T. C. PRATT. Operations  
supracondylar amputations for gangrene.

## CARNEY HOSPITAL

## Tuesday

## OBSTETRICS AND GYNECOLOGY

- LOUIS E. PRANSKY and associates—*g.* Operative clinic.  
LOUIS E. PRANSKY and associates—*g.* Dry clinic.

## Wednesday

## GENERAL SURGERY

- WILLIAM E. BROWN, W. R. MACATELAND, ROGER C.  
GRAVER, and A. MCK. FRASER—*g.* Operations.  
Staff—*g.* Dry clinic.

## GENITO-URINARY SURGERY

- Staff—*g.* Dry clinic.

## ORTHOPEDIC SURGERY

- Staff—*g.* Dry clinic.

## Thursday

## GENERAL SURGERY

- WILLIAM E. BROWN, W. R. MACATELAND, ROGER C.  
GRAVER, and A. MCK. FRASER—*g.* Operations.  
Staff—*g.* Dry clinic.

## GENITO-URINARY SURGERY

- Staff—*g.* Dry clinic.

## ORTHOPEDIC SURGERY

- Staff—*g.* Dry clinic.

## Friday

## GENERAL SURGERY

- WILLIAM E. BROWN, W. R. MACATELAND, ROGER C.  
GRAVER, and A. MCK. FRASER—*g.* Operations.

## ROBERT BRECK BRIGHAM HOSPITAL

## Wednesday

## ORTHOPEDIC SURGERY

- Staff— Symposium. End-results on rehabilitation of  
chronic arthritis, prevention of deformities and early  
rehabilitation, results in correction of flexion deformity  
of knee, arthroplasty in upper extremity, open or  
closed of arthritic disabilities of the foot.

## Days to be Announced

## ORTHOPEDIC SURGERY

- Staff—*g.* Operative clinic. Posterior capsuloplasty for  
correction of flexion deformity of knee; arthroplasty of  
elbow for ankylosis.

## MASSACHUSETTS MEMORIAL HOSPITALS

*Monday*

## THORACIC SURGERY

J W STRIEDER—2 Symposium

*Tuesday*

## GENERAL SURGERY

HOWARD M CLUTE and staff—8 Operative clinic  
FRANK E BARTON—10 Symposium Management of blood bank

PHILLIPS L BOYD—10 Dry clinic Lymphogranuloma venereum with rectal involvement

THOMAS J ANGLE—2 Symposium Cancer of the breast

FRANK E BARTON—2 Transfusion service

## GENITO URINARY SURGERY

SAMUEL N VOSE and staff—9 Operative clinic

## OTORHINOLARYNGOLOGY

HAROLD L BABCOCK and LEIGHTON F JOHNSON—2 Operative and dry clinic

*Wednesday*

## GENERAL SURGERY

HOWARD M CLUTE and staff—8 Operative clinic  
GEORGE LEVENE and EGON G WISSING—9 30 Demonstration X ray examination of the rectum and sigmoid with special reference to the lateral viewHOWARD M CLUTE—10 Symposium Stomach surgery  
FRANK E BARTON—2 Transfusion service

## GENITO-URINARY SURGERY

SAMUEL N VOSE—9 Symposium Management of obstructing prostate

## THORACIC SURGERY

J W STRIEDER—2 Operative and dry clinic

## ORTHOPEDIC SURGERY

LOUIS G HOWARD and staff—9 Operative and dry clinic

## OPHTHALMOLOGY

WILLIAM D ROWLAND—9.30 Dry clinic

## OTORHINOLARYNGOLOGY

LEIGHTON F JOHNSON—2 Dry clinic Mediastinitis, 3 cases, 2 cures (with Howard M Clute), endaural repair of postauricular fistula, 3 cases, osteomyelitis of frontal bone, Lempert's operation, endaural fenestration for otosclerosis

*Thursday*

## GENERAL SURGERY

HOWARD M CLUTE and staff—8 Operative clinic  
MILO C GREEN, CHESTER S KEEFER, HOWARD M CLUTE, HOLLIS L ALBRIGHT, SAMUEL N VOSE, and LEIGHTON F JOHNSON—10 Use of sulfonamide group in surgery  
ARTHUR L HANRAHAN—10 Operative and dry clinic Treatment of varicose veins and ulcers

## OBSTETRICS AND GYNECOLOGY

C WESLEY SEWALL and staff—8 Operative and dry clinic, ward walk

C WESLEY SEWALL and staff—2 Symposium Obstetrical  
JOHN J ELLIOTT A ten year study of bleeding in the third trimester of pregnancy

OWEN C MULLANEY Prenatal and postnatal care

JOHN C V FISHER. A ten-year survey of cesarean section

MAX DAVIS Physiology and clinical application of testosterone

KENNETH W SEWALL A twenty-year survey of eclampsia

HERMAN C PETTERSON Modern care of the newborn

## ORTHOPEDIC SURGERY

LOUIS G HOWARD, ALBERT B FERGUSON, and associates—9 Discussion of bone tumors

## OPHTHALMOLOGY

WILLIAM D ROWLAND and RALPH H HOPKINS—2 Operative clinic

*Friday*

## GENERAL SURGERY

HOWARD M CLUTE and staff—9 Operative clinic

## GENITO-URINARY SURGERY

SAMUEL N VOSE—9 Operative and dry clinic

## UNITED STATES MARINE HOSPITAL

*Tuesday*

## GENERAL SURGERY

R L WAUGH and staff—8 Operative clinic Hernioplasty, indirect, direct, and femoral, appendectomy, ligation of saphenous vein and hemorrhoidectomy

R L WAUGH and staff—11 Dry clinic Appendicitis, intestinal parasites, and terminal ileitis

## FRACTURES AND OTHER TRAUMAS

R L WAUGH and staff—8 Operative clinic Internal derangement of knee joint, bunion, closed treatment, double pin method, fracture both bones of leg, open treatment, vitalium plate, both bones forearm

R L WAUGH and staff—1 Dry clinic Skeletal traction and countertraction methods applicable to ordinary extension splints in the treatment of fractures of lower extremity, vitalium in fractures, injuries of the wrist and rupture of biceps brachii

*Friday*

## GENERAL SURGERY

R L WAUGH and staff—9 Operative clinic Hernioplasty, indirect, direct and femoral, appendectomy, ligation of saphenous vein and hemorrhoidectomy

R L WAUGH and staff—11 Dry clinic Appendicitis, intestinal parasites, and terminal ileitis

## FRACTURES AND OTHER TRAUMAS

R L WAUGH and staff—9 Operative clinic Internal derangement of knee joint, bunion, closed treatment, double pin method, fracture both bones of leg, open treatment, vitalium plate, both bones forearm

R L WAUGH and staff—1 Dry clinic Skeletal traction and countertraction methods applicable to ordinary extension splints in the treatment of fractures of lower extremity, vitalium in fractures, injuries of the wrist and rupture of biceps brachii.

Daily—9 to 5

## SCIENTIFIC EXHIBIT

- JOSEPH GOODMAN. Pathogenic fungi in foot infections.  
 J. F. FRIEDMAN. Malignant diseases before and after treatment by radiation.  
 ABRAHAM RUDY and S. R. MYLLNER. Neurogenic bladder in diabetes mellitus.  
 JULIUS LOWAN. Action of antitumor drugs on the gastro-intestinal and genito-urinary tracts.  
 S. A. ROSSER. Urography and cystography.  
 W. S. ALTMAN and A. L. HIRSH. 1907. Cholangiography.  
 L. NATTA and Dr. TSOVA. Cysts and tumors of mouth and jaw.  
 JULIUS LOWAN. Cerebral arteriography.

## FAULKNER HOSPITAL

Wednesday

## GENERAL SURGERY

- E. L. YOCUM, A. R. KIMPTON, F. O. BALCH, H. K. SOWLES, R. F. SKELDON, E. E. O'NEIL, R. S. TITUS, and R. J. HOFFERMAN—4. Operative clinic.  
 S. C. WOODY—2. Anesthetics exhibits.  
 J. B. HALLARD—2. Pathological specimens, slides.  
 E. L. YOCUM, F. O. BALCH, Dr. JETTER, A. R. KIMPTON, H. K. SOWLES, R. F. SKELDON, R. J. HOFFERMAN, R. S. TITUS, Dr. STRAUSS, Dr. MALONEY and E. E. O'NEIL—2. Dry clinic.  
 HARRY MORRISON—2. X ray demonstrations.

Thursday

## ORTHOPEDIC SURGERY

- E. G. BRACKETT, H. C. MARBLE, O. M. MORRISON, J. D. ADAMS, and OTTO J. HERMANN—2. Operative clinic.  
 HARVEY MORRISON—4. X ray demonstrations.  
 E. G. BRACKETT, A. P. ATKINER, J. L. DOWNEY, H. C. MARBLE, OTTO J. HERMANN, HARVEY MORRISON, J. D. ADAMS, and H. L. JOHNSON—2. Dry clinic.  
 JOHN HOSKINS, C. G. MITCHELL, R. H. SMITHSON, Dr. WHITE, E. E. O'NEIL, H. C. MARBLE, and J. S. HOSKINS—4. Symposia. Cannulae.

## BEVERLY HOSPITAL

Thursday

## GENERAL SURGERY

- Staff—9. Demonstration of newly constructed operating room with elimination of explosion and fire hazards.

## FRACTURES AND OTHER TRAUMAS

- PET. P. JOHNSON, JOHN D. ADAMS, and RICHARD E. ALT—Dry clinic. Discussion by CLAY RAY MITCHELL, ROBERT H. KENNEDY and L. EDWARD W. BANCROFT.

## MALDEN HOSPITAL

Friday

## GENERAL SURGERY

- I. J. WALLER and staff—9. Operations (Gastro-intestinal).  
 I. J. WALLER and staff—2. Dry clinic.

## OBSTETRIC AND GYNECOLOGY

- NICHOLAS A. GALLAGHER—9. Operations Gynecological.

- B. E. GREENBERG. Use of cholinergic and adrenergic medication for ureteral stone passage.  
 H. A. KONTOFF. Hospital statistics on urinary lithiasis.  
 J. H. LIPPSTON. Clearance of infection in stone cases after operation.  
 D. B. STRAUSS. Diagnosis of calyceal calcifications.  
 H. A. KONTOFF. Renal tumor statistics of the hospital.  
 Demonstration. Surgical specimens of renal tumors with pyelographic and microscopic data.  
 E. G. CHARTERIS—Operation. Excision of renal tumor.  
 Staff—1. Dry clinic.  
 M. L. BROOKE. Fractional pyelography.  
 J. H. LIPPSTON. Sulfonamide drugs in surgical wounds and postoperative infections.  
 B. E. GREENBERG. Methylene blue treatment for tuberculous of the bladder.  
 L. L. PIERCE. Renal injury from sulfathiazole and sulfa pyridine, nature of the lesion.  
 D. B. STRAUSS. Undescended testicle age groups.  
 M. L. BROOKE. Urological study of excretory cases.  
 Dr. FRIEDMAN. Denervation of the kidney—results of 300 cases.  
 B. E. GREENBERG. Organization and function of the Rhy clinic.  
 NATHAN CHARTERIS. Hypertensive disease in urology.

Friday

## GENERAL SURGERY

- Staff—9. Dry clinic.  
 C. G. MITCHELL. Results of surgery of colon neoplasms classified according to extent of lesion.  
 L. E. BARRETT. Pitfalls in diagnosis of carcinoma of stomach, observations in 300 cases.  
 C. G. MITCHELL. Results of surgery of gastric neoplasms classified according to extent of lesion.  
 I. T. NATHANSON. Surgical management of lymph nodes in cancer surgery.  
 K. PINKER. Differential diagnosis of gastric ulcer by radiography.  
 JACOB PINKER—9. Operation. Colon resection.  
 C. G. MITCHELL—9. Operation. Gastric resection.  
 Staff—2. Dry clinic.  
 A. M. SELIGMAN. Vitamin K in treatment of hypoprothrombinemia in infants.  
 J. J. MICHAELS and Miss E. CORNELL. Psychiatric conditions in surgical patients.  
 B. RICHMAN. The surgical treatment of angina pectoris.  
 S. A. ROSSER. Diagnosis of non-calcified dermoid cysts.  
 A. M. SELIGMAN. Cardiovascular agents.  
 H. L. CANNIT. Surgical management of pulmonary tuberculosis.  
 ALFRED THURM. Thoracic esophageal diverticulum.

## OTORHINOLARYNGOLOGY

- Staff—9. Dry clinic.  
 SAMUEL CLIVE. Tuberculous laryngitis.  
 OSCAR HIRSCH. Sphenoid approach through subnasal septum.  
 A. J. GORREY. Lempert's simple and radical mastoid operations.  
 S. W. GARDNER. Transseptal approach for dacryocystitis.  
 H. F. FRIEDMAN. Radiation for carcinoma of larynx by the Costrand method.  
 BENJAMIN RICHMAN. Cervicofacial sinus thrombosis.  
 LOUIS M. FRIEDMAN. Costrand radiation therapy for carcinoma of larynx, end results. Lempert technique for simple and radical mastoidectomy.  
 LOUIS M. FRIEDMAN. Operation Lempert for mastoiditis.

M G KARP—10.45 Fractures about the elbow in childhood.  
Staff—11 15 Congenital malformations

*Daily—2 to 5*

#### SCIENTIFIC EXHIBIT

Exhibit of pathological specimens, x-rays, photographs, and charts from the surgical, orthopedic and neuro surgical services

### NEW ENGLAND MEDICAL CENTER

JOSEPH H PRATT DIAGNOSTIC HOSPITAL

*Monday*

#### GENERAL SURGERY

Staff—2 Dry clinic

JOSEPH H PRATT Surgical problem in pancreatic disease.

WILLIAM DAMESHEK. Indications for splenectomy, case reports

JOHN D ADAMS Orthopedic subject, to be announced

WALTER E GARREY Peritoneoscopy

*Tuesday*

#### GENERAL SURGERY

Staff—2 Dry clinic

C H LAWRENCE Masculinizing tumors

R H BETTS Subject to be announced

WILLIAM M SHEDDEN Subject to be announced

EDWARD T WHITNEY Subject to be announced

*Wednesday*

#### GENERAL SURGERY

Staff—2 Dry clinic

RICHARD H. OVERHOLT Operability of primary carcinoma of the lung

L E PHANEUF Subject to be announced

S J THANNHAUSER. Liver function tests as an aid to gall bladder surgery

H E MACMAHON Subject to be announced

### BOSTON FLOATING HOSPITAL

*Thursday*

#### GENERAL SURGERY

RICHARD WAGNER and W S LEVENSON—2 Endocrinology and surgery

DR. McDONALD and R G FREEMAN—2 Appraisal of the host, nutrition, personality

DR. McDONALD, W S LEVENSON, DR. WERTHESEN, and H E MACMAHON—2 Adrenal dysfunction

#### GENITO-URINARY SURGERY

H.A CHAMBERLIN—2 Genito-urinary surgery in children

#### THORACIC SURGERY

RICHARD H OVERHOLT, R. H BETTS, and DR. WELLER—2 Tidal drainage, lung abscess

#### OTORHINOLARYNGOLOGY

W A. MACCOLL—2 Tonsils and adenoids, indications for removal.

BOSTON DISPENSARY—PRATT CLINIC

*Days to be Announced*

#### OTORHINOLARYNGOLOGY

GEORGE KELEMEN Pathogenesis of traumatic cholesteatoma, lantern slides, surgery of the tonsil after middle life, pathways of infection in the ear, lantern slides

PHILIP E MELTZER. Surgical anatomy of the temporal bone

### UNITED STATES NAVAL HOSPITAL

*Tuesday*

#### GENERAL SURGERY

J J A McMULLIN and staff—9 Operations

JAMES J REGAN—9 Demonstrations of technique used in flight physical examinations, with discussion of United States Naval requirements

#### OTORHINOLARYNGOLOGY

CHARLES H ALLMAN—9 Dry clinic Bronchoscopy for bronchiectasis, pulmonary abscess and postoperative atelectasis, synopsis of case histories and accomplishments

*Wednesday*

#### GENERAL SURGERY

LAWRENCE J MCCARTHY and staff—9 Operations

THOMAS H PETERSON—9 Shoulder injuries, discussion of case histories, x-ray findings

WALTER E GARREY—9 Dry clinic Circulatory diseases of the extremities, case histories

*Thursday*

#### GENERAL SURGERY

WALTER E GARREY and staff—9 Operations

LAWRENCE J MCCARTHY and WALTER E GARREY—9 Gastro intestinal clinic Partial gastrectomy for pyloric obstruction with a synopsis of case histories

#### GENITO-URINARY SURGERY

E ROSS MINTZ—9 Dry clinic Presentation of urological cases with histories and x-ray findings

*Friday*

#### GENERAL SURGERY

THOMAS H PETERSON—9 Operations

#### OBSTETRICS AND GYNECOLOGY

JOSEPH B DOYLE—10 Colored moving pictures of spinal anesthesia in obstetrics, discussion of case histories

### COLLIS P HUNTINGTON MEMORIAL HOSPITAL

*Monday*

#### GENERAL SURGERY

Staff—2 15 Dry clinic

JOSEPH C AUB Recent advances in our knowledge of bone diseases

CHANNING C SIMMONS Malignant tumors of bone



MASSACHUSETTS EYE AND EAR  
INFIRMARY

## Monday

## OPHTHALMOLOGY

F. H. VERBOFF and WILLIAM P. BEETMAN— 5. Dry  
clinic. Cataract surgery

## Tuesday

## OPHTHALMOLOGY

PAUL A. CHANDLER, FRED S. THORNT, T. YUVE GUNDE  
SEN and PAUL G. HARRIS— 9. Operations.  
PAUL A. CHANDLER— 5. Glaucoma, indications for  
operation.  
SAMUEL T. CLARKE— 5. Goniotomy medical treat  
ment.

## Wednesday

## OPHTHALMOLOGY

WILLIAM P. BEETMAN, SAMUEL H. WILKINS, BRENDAN D.  
LEAHY and D. W. G. COOBY— 9. Operations.  
E. B. DUFFY— 15. Strabismus, orthoptic training.  
VIRGIL G. CASTER— 5. Strabismus, operative treatment.

## Thursday

## OPHTHALMOLOGY

EDWIN B. GOODALL, RALPH H. RUGGER, MERRILL J.  
KING, and HERMA GROSSMAN— 9. Operations.  
MERRILL J. KING— 15. Dry clinic. Retinal separation.  
BRENDAN D. LEAHY— 15. Dry clinic. Keratoplasty

## Friday

## OPHTHALMOLOGY

BENJAMIN SACHS and JOHN G. JENNINGS— 9. Operations.  
Staff— 9. Demonstrations.  
WILLIAM P. BEETMAN. Slit Lamp  
GARRETT L. SCLAVAK. Perimetry  
VIRGIL G. CASTER. Neuro-ophthalmology  
SAMUEL T. CLARKE. Gonioscopy  
T. L. TERRY— 15. Dry clinic and lantern demonstra  
tions of pathological specimens.  
V. H. KASANJIAN— 15. Ophthalmoplastic surgery

## Days to be Announced

## OTORHINOLARYNGOLOGY

A. S. MACMILLAN. Interpretation of x-rays and mastoid  
x-rays.  
L. O. RICHARDS. Bronchoscopy problems.  
C. T. PORTER. Orbital abscess, diagnosis and treatment.  
L. A. SCHALL. Cancer of the nose and sinuses. Surgical  
cancer.  
G. B. FRED. Osteomyelitis of the frontal bone.  
H. G. TOWSE. Allergy otolaryngological considerations.  
P. E. METZGER and C. E. JORDAN. The larynx.  
operation.  
RUTH GILDER. The deaf child.  
V. H. KASANJIAN. Rhinoplastic surgery.  
PHILIP MITCHELL. Labyrinthectomy review of cases.  
C. M. KOS. Meningitis, review of cases.

## SCIENTIFIC EXHIBIT

T. L. TERRY. Pathological laboratory open for inspection.  
D. W. G. COOBY. How laboratory and library open for  
inspection.

## CHILDREN'S HOSPITAL

## Tuesday

## GENERAL SURGERY

W. E. LADD and associates— 10. Dry clinic. Surgical  
diseases of the gastro-intestinal tract in childhood.  
Atresia, stenosis, and malrotation. Pyloric stenosis. In  
testinal obstruction, appendicitis, followed by questions and  
discussion.

## GENITO-URINARY SURGERY

W. E. LADD and associates— 9. Dry clinic. Surgical d  
iseases of the genito-urinary tract in infancy and child  
hood. Embryoma, malformations, ectropion and ep  
ispadias, followed by questions and discussion.

## ORTHOPEDIC SURGERY

F. R. OWER and associates— 9. Operations.

## Wednesday

## GENERAL SURGERY

W. E. LADD and associates— 9. Operations.

## ORTHOPEDIC SURGERY

F. R. OWER and associates— 9. Dry clinic.  
W. A. ELLISTON— 9. Study in bone growth and resorp  
tion of the epiphyseal plate.  
L. M. McDONNELL— 10. Equalization of leg length  
by lengthening.  
P. W. H. GIESSENBERGER— 9. Tuberculosis of bone.  
A. H. BRANTNER— 10. Arthrodesis of the foot  
in spastic paralysis.  
Staff— 9. Symposium on infantile paralysis, operative  
treatment.

## Thursday

## GENERAL SURGERY

W. E. LADD and associates— 9. Dry clinic. Plastic surger  
y in childhood. Harlip and cleft palate. Burns, early as  
late treatment. Hands, syndactylism and polydactylism.  
Plastic for malformations. Bowel, nose, followed by ques  
tions and discussion.

## THORACIC SURGERY

W. E. LADD and associates— 10. Dry clinic. Chro  
nic suppuration, heart, patent ductus arteriosus.  
Lik questions and discussion.

## NEUROSURGERY

W. E. LADD and associates— 10. Dry clinic.

## ORTHOPEDIC SURGERY

F. R. OWER and associates— 9. Operations.

## Friday

## GENERAL SURGERY

W. E. LADD and associates— 9. Operations.

## ORTHOPEDIC SURGERY

F. R. OWER and associates— 9. Dry clinic.  
M. G. KATZOFF— 9. Early treatment of club-foot.  
R. H. MORRIS— 9. Treatment of the difficult club-foot.  
F. R. OWER— 10. Treatment of congenital dislocation of  
the scapula.  
DR. GREEN— 10. Osteochondritis dissecans.

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 CHARLES E. DUNLAP. Cardiogenic agents.  
 CLIFFORD C. FRANKLIN. Industrial cancer.

### Thursday

#### GENERAL SURGERY

Staff—A. S. Dry clinic

GRANTLEY W. T. FIOR. Choice of treatment in cancer of the oral cavity.  
 D. VAN WEINBERGER. Changes in the oral mucosa membrane due to vitamin deficiency.  
 SHELLE WARRER. Treatment of leukemia by radio-active substances.  
 IRA T. NATHANSON. Relation of the hormones to the Hyphant diseases.

### PONDVILLE HOSPITAL

#### Wednesday

#### GENERAL SURGERY

E. M. DALAKO and associates—p. Operative and dry clinics.  
 SHELLE WARRER and associates—p. Demonstration Pathological.  
 CHARLES DUNLAP and associates—p. Exhibit Bone tumors.

#### OBSTETRICS AND GYNECOLOGY

JOE V. MITOS and associates—p. Operative and dry clinic Gynecological cancer.

#### GENITO-URINARY SURGERY

ROGER C. GRAVES—p. Operative and dry clinic Urological cancer.

### SALEM HOSPITAL

#### Tuesday

#### GENERAL SURGERY

W. G. PHILLIPS, DONALD A. NICKERSON, and S. A. WILSON—p. Dry clinic: Uses and abuses of laboratory and roentgenological procedures in abdominal surgery.  
 E. L. FRIEDSON—Prostatic surgery with some newer methods of diagnostic approach.

#### Friday

#### GENERAL SURGERY

Staff—Clinical pathological conference.

### EVANGELINE BOOTH MATERNITY HOSPITAL

#### Days to be Announced

#### OBSTETRICS AND GYNECOLOGY

A. K. PAINE, W. J. McDONALD, H. S. FINKE, M. G. BEULKE, J. E. HOPKINS, D. C. GOLDFARB, A. A. LEVY, L. ALBERT, S. ELLIS, J. TAN AKOFF and S. SEDWELL. Operative and dry clinics.

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